Original Article

# Isolation Rate and Clinical Significance of Uropathogens in Positive Urine Cultures of Hemodialysis Patients

**Katerina G Oikonomou, Adib Alhaddad**

Department of Medicine, NYU Lutheran Medical Center, New York University School of Medicine, Brooklyn Campus, Brooklyn, NY, USA

## Abstract

**Background:** Hemodialysis (HD) patients are known to be vulnerable to infections. However, there are limited data on the urine microbiology spectrum among patients with end-stage renal disease and on the development of antimicrobial resistance of uropathogens in these patients. **Materials and Methods:** A single-center, retrospective study was conducted to assess the spectrum and antimicrobial resistance profile of microorganisms isolated in urine cultures of HD patients who were hospitalized between September 2008 and August 2015 with an admitting diagnosis of fever, sepsis, or urinary tract infection. Characteristics of patients were recorded, and associations between the aforementioned parameters were assessed with Fisher's exact test. **Results:** We included 75 HD patients (33 males, mean age 73.6 ± 16.6 years) with positive urine cultures. Despite urine culture positivity, the urinary tract was the confirmed source of infection in only 31 (41.3%) patients. Among the different pathogens, *Escherichia coli* was the predominant microorganism. Identification of *E. coli* as the involved uropathogen was associated neither with a growth of $\geq 10^5$ CFU/ml, presence of fever, sepsis, urinary catheter use nor with higher antimicrobial resistance. *E. coli* growth, however, was significantly associated with polycystic kidney disease ($P = 0.027$). Extended antimicrobial resistance was noted in 29 (38.7%) patients but was associated neither with higher incidence of fever or sepsis nor with urinary catheter use. **Conclusions:** In our series of HD patients with positive urine cultures, the isolation rates of different uropathogens do not seem to differ from the most commonly encountered ones in nondialysis patients although resistance to antimicrobials may be more frequently observed.

**Keywords:** Hemodialysis, microorganisms, urinary tract infection

## Introduction

Hemodialysis (HD) patients are vulnerable to infections due to impaired immune response.[1-3] The most common sources of infection are HD catheters, pneumonia, and urinary tract infections (UTIs).[4-7] HD patients are prone to UTI due to low urine volume, bladder stasis, and frequent hospitalizations, which lead to multidrug-resistant (MDR) microorganisms.[8-10]

There are limited data on the urine microbiology in patients with end-stage renal disease (ESRD) or the latter's role in the development of antimicrobial resistance. The aim of this study was to identify the most common causative agents for UTI and the patterns of antimicrobial resistance in HD patients.

## Materials and Methods

Seventy-five HD patients (33 males, mean age 73.6 ± 16.6 years) with positive, noncontaminated urine culture, with growth of a single microorganism, who required acute inpatient care for an admission diagnosis of fever, sepsis, or UTI between September 2008 and August 2015 were retrospectively identified. The study was approved by the Institutional Review Board of our institution.

Fever was defined as a body temperature of 100.4°F or 38°C. The detection of bacteria at a colony count threshold of $\geq 10^5$ bacteria/ml in urine culture was used as the diagnostic standard for UTI. Sepsis was defined as the presence (probable or documented) of infection together with systemic manifestations of infection according to the Infectious Diseases Society of America guidelines.

**Address for correspondence:** Dr. Katerina G Oikonomou, Department of Medicine, New York University School of Medicine (Brooklyn Campus), NYU Lutheran Medical Center, 150 55th Street, Brooklyn, NY 11220, USA.
E-mail: katerina.oikonomou@nyumc.org

**Access this article online**

Quick Response Code:

**Website:** www.jgid.org

**DOI:** 10.4103/0974-777X.204691



**How to cite this article:** Oikonomou KG, Alhaddad A. Isolation rate and clinical significance of uropathogens in positive urine cultures of hemodialysis patients. J Global Infect Dis 2017;9:56-9.

Patients were included if they were older than 18 years, were on HD for more than 1 month, and had a urinary output more than 30 ml between two HD sessions. More than 3 microorganisms in urine culture were considered to be colonizers and these patients were excluded from the study. A clean catch midstream specimen was obtained for urine culture in 49 patients. In 24 patients, sample was collected with urethral catheterization and 2 patients had chronic indwelling urinary catheter. In these patients, urine specimen was obtained through the port of the drainage system after placement ($n = 24$) or replacement ($n = 2$) of the catheter before urine specimen collection. Patients with a suprapubic catheter were excluded from the study. Patients for whom urine cultures were obtained after antibiotic initiation or 24 h after admission were excluded from the study.

All urine samples were inoculated using the standard procedure of surface streaking method on culture media and incubated at 37°C for 24 h. Samples were inoculated on culture media by making a single line streak down the middle of the plate from top to bottom. Then, the culture plate was filled with streaking lines to produce isolated colonies. Smears obtained from the bacterial colonies on the culture media were further evaluated by Gram stain. The isolated organisms were identified and the growth was calculated in colony-forming units per milliliter (CFU/ml). Susceptibility to various antimicrobial agents was tested by the disk diffusion method.

Demographic, clinical, and laboratory characteristics of patients were recorded, including age, gender, cause of ESRD, presence of fever, sepsis, urinary catheter, urine culture isolates, growth (CFU/ml), and presence of resistance, as well as source of infection. Interrelations of the aforementioned parameters were assessed with Fisher's exact test. The level of statistical significance was set at $P < 0.05$. Statistical analysis was performed using SPSS (version 17, SPSS Inc, Chicago, IL, USA).

## Results

All demographic characteristics of patients included in the study are presented in Table 1. Notably, despite urine culture positivity, the urinary tract was the confirmed source of infection in only 31 out of 75 (41.3%) patients. There was no significant association between the Gram staining group of microorganism (Gram-positive vs. Gram-negative) and the underlying cause of ESRD (diabetes mellitus, hypertension, glomerulopathy). Among different pathogens, *Escherichia coli* was the predominant microorganism causing UTI in HD patients [Table 2], followed by *Enterococcus* spp. Identification of *E. coli* as the involved uropathogen was associated neither with a growth of $\geq 10^5$ CFU/ml, presence of fever, sepsis, urinary catheter use nor with higher antimicrobial resistance. However, *E. coli* growth was significantly associated with the presence of polycystic kidney disease (PKD; $P = 0.027$).

Extended antimicrobial resistance was noted in 29 (38.7%) patients [Table 3] but was associated neither with higher incidence of fever or sepsis nor with urinary catheter use. Extended-spectrum β-lactamase-producing *E. coli* was isolated in the urine cultures in the majority of patients with MDR microorganisms (41.4%), followed by vancomycin-resistant *Enterococci* (24.1%).

**Table 1: Hemodialysis Patients' Characteristics, Clinical and Laboratory Parameters**

| Characteristics | *n* (%) |
|---|---|
| Age (years), mean±SD | 73.6±16.6 |
| <65 | 20 (26.7) |
| ≥65 | 55 (73.3) |
| Gender | |
| Male | 33 (44) |
| Female | 42 (56) |
| Diabetes mellitus | 34 (45.3) |
| Hypertension | 60 (80) |
| Glomerulopathy | 1 (1.3) |
| Polycystic kidney disease | 4 (5.3) |
| Other chronic kidney disease causes | 11 (14.7) |
| Urinary catheter use | 28 (60.9) |
| Fever | 10 (13.3) |
| Sepsis | 20 (26.7) |
| Infection source | 72 (96) |
| Respiratory | 15 (20) |
| Skin and soft tissue | 2 (2.7) |
| Bone and joint | 1 (1.3) |
| Bacteremia, catheter-related | 6 (8.0) |
| Bacteremia, noncatheter-related | 9 (12) |
| Gastrointestinal | 8 (10.7) |
| Urinary tract infection | 31 (41.3) |
| Colony-forming units/ml $\geq 10^5$ | 44 (48.9) |

SD: Standard deviation

**Table 2: Isolated Microorganisms in Urine From Hemodialysis Patients**

| Microorganism | Dialysis patients, *n* (%) |
|---|---|
| *E. coli* | 22 (29.3) |
| *Klebsiella* | 8 (10.7) |
| *Pseudomonas* | 6 (8.0) |
| *Enterobacter* | 6 (8.0) |
| *Proteus* | 5 (6.7) |
| *Enterococcus* | 9 (12) |
| *Staphylococcus* | 6 (8.0) |
| Streptococcus | 3 (4.0) |
| Other Gram-negative | 5 (6.7) |
| Other Gram-positive | 2 (2.7) |
| *Candida* | 3 (4.0) |
| Total | 75 (100) |

*E. coli*: *Escherichia coli*

## Discussion and Conclusions

In this study, we aimed to identify the most common uropathogens in HD patients with UTI and further determine whether ESRD is associated with the development of antimicrobial resistance of uropathogens in these patients. In general population, *E. coli* is the most common organism

**Table 3: Patterns of Antimicrobial Resistance of Uropathogens in Hemodialysis Patients**

| Resistant microorganisms | Dialysis patients, *n* (%) |
|---|---|
| *E. coli* ESBL | 12 (41.4) |
| *E. coli* MDR | 1 (3.4) |
| *Klebsiella* carbapenemase | 2 (6.9) |
| VRE | 7 (24.1) |
| MRSA | 5 (17.2) |
| *Candida* spp. resistant to fluconazole | 2 (6.9) |
| Total | 29 (100) |

ESBL: Extended-spectrum beta-lactamase, MDR: Multidrug-resistant, VRE: Vancomycin-resistant *Enterococcus*, MRSA: Methicillin-resistant *Staphylococcus aureus*, *E. coli*: *Escherichia coli*

involved in UTI and this is observed both in the outpatient setting and in hospitalized patients.[11-13] In a previous study by Jung *et al*., it was reported that the most common cause of acute pyelonephritis in chronic renal failure patients was *E. coli* (58.3%, *n* = 293), followed by *Klebsiella pneumoniae*.[1] Similar findings were also shown in the study of Jadav *et al*., where *E. coli* was the predominating uropathogen in HD patients,[14] while in the study of Jaiswal *et al*., *E. coli* was the most common microorganism in male HD patients.[15] D'Agata *et al*. reported that *Candida* spp. was the most common pathogen implicated in nosocomial UTI in HD patients.[16] Our findings concur with the bulk of existing literature. In addition, we further demonstrate that *E. coli* growth is significantly associated with PKD. Autosomal dominant PKD is responsible for about 5% of ESRD.[17] Infection of a cyst can occur from bacteremia or the urine in an ascending manner.[17] Patients with PKD develop more serious complications, including intrarenal or perinephric abscess, and as such, there should be a higher index of suspicion for the prompt diagnosis of UTI and a lower threshold for initiation of appropriate antimicrobial treatment.[4,15]

Chronic renal failure did not seem to alter the isolation rates of different uropathogens or their patterns of susceptibility to antimicrobials in a previous study.[1] The presence of diabetes mellitus was also reported to have no effect on the types of uropathogens.[1,18] In our study, there was also no association between diabetes mellitus and other causes of ESRD (hypertension and glomerulopathy) with the types of microorganisms isolated. In a comprehensive attempt to evaluate potential risk factors associated with antimicrobial-resistant urinary pathogens, Faine *et al*. confirmed the significant role of chronic HD and also identified male sex and nursing home residence as additional clinical factors associated with the identification of MDR urinary pathogens.[19]

In our series, a high percentage of antimicrobial resistance was observed (38.7%); however, there was no comparison between HD patients and patients without renal disease (controls) in our cohort. Additional limitations of our study include the retrospective data collection, the relatively small number of patients, and the fact that data were obtained from patients admitted to a single medical institution. Further studies are required for assessment of differences in patients and microbiologic characteristics of pathogens in various healthcare settings. Results of the study may also have been affected by inclusion of patients with urinary catheter. However, only patients with documentation of aseptic insertion/replacement of urinary catheter were included in the study.

Our study has several implications for clinical management of HD patients with UTI. First of all, although same microorganisms are observed in HD and general population, there are higher rates of MDR microorganisms in HD patients. Therefore, physicians should be vigilant for early diagnosis and initiation of broad-spectrum antibiotic regimens for treatment of UTI in these patients. In addition, implementation of infection control surveillance in HD setting is of vital significance due to rapidly increasing antimicrobial resistance and relatively limited antimicrobial options.

In the era of increasing emergence and spread of antimicrobial resistance, the appropriate choice of antibiotics for the treatment of UTI in patients with renal failure is challenging.[20] Large multicenter studies are required to further address the impact of ESRD on the antimicrobial susceptibility of uropathogens and to guide appropriate choice of antibiotic coverage.[1,19]

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Jung YS, Shin HS, Rim H. The influence of chronic renal failure on the spectrum and antimicrobial susceptibility of uropathogens in community-acquired acute pyelonephritis presenting as a positive urine culture. BMC Infect Dis 2011;11:102.
2. Albuquerque SE, Cavalcante Rde S, Ponce D, Fortaleza CM. Epidemiology of healthcare-associated infections among patients from a hemodialysis unit in Southeastern Brazil. Braz J Infect Dis 2014;18:327-30.
3. Chonchol M. Neutrophil dysfunction and infection risk in end-stage renal disease. Semin Dial 2006;19:291-6.
4. Rault R. Symptomatic urinary tract infections in patients on maintenance hemodialysis. Nephron 1984;37:82-4.
5. Keane WF, Shapiro FL, Raij L. Incidence and type of infections occurring in 445 chronic hemodialysis patients. Trans Am Soc Artif Intern Organs 1977;23:41-7.
6. Dobkin JF, Miller MH, Steigbigel NH. Septicemia in patients on chronic hemodialysis. Ann Intern Med 1978;88:28-33.
7. Nsouli KA, Lazarus M, Schoenbaum SC, Gottlieb MN, Lowrie EG, Shocair M. Bacteremic infection in hemodialysis. Arch Intern Med 1979;139:1255-8.
8. Stamm WE. Measurement of pyuria and its relation to bacteriuria. Am J Med 1983;75:53-8.
9. Tokars JI, Miller ER, Stein G. New national surveillance system for hemodialysis-associated infections: Initial results. Am J Infect Control 2002;30:288-95.
10. Fasolo LR, Rocha LM, Campbell S, Peixoto AJ. Diagnostic relevance of pyuria in dialysis patients. Kidney Int 2006;70:2035-8.
11. Gilbert DN. Urinary tract infections in patients with chronic renal insufficiency. Clin J Am Soc Nephrol 2006;1:327-31.
12. Hooton TM. The current management strategies for community-acquired

urinary tract infection. Infect Dis Clin North Am 2003;17:303-32.
13. Behzadi P, Behzadi E, Yazdanbod H, Aghapour R, Akbari Cheshmeh M, Salehian Omran D. A survey on urinary tract infections associated with the three most common uropathogenic bacteria. Maedica (Buchar) 2010;5:111-5.
14. Jadav SK, Sant SM, Acharya VN. Bacteriology of urinary tract infection in patients of renal failure undergoing dialysis. J Postgrad Med 1977;23:10-8.
15. Jaiswal S, Das R, Sharma S, Paudel P, Lamichhane SR. Bacteriological study of urinary tract infection in male patients undergoing dialysis due to chronic kidney disease in tertiary care hospitals in Nepal. Res Rev J Life Sci 2013;3:8-9.
16. D'Agata EM, Mount DB, Thayer V, Schaffner W. Hospital-acquired infections among chronic hemodialysis patients. Am J Kidney Dis 2000;35:1083-8.
17. Pien FD, Berman SJ. Infections in patients with chronic renal failure. Infect Dis Clin North Am 2001;15:709-8.
18. Bonadio M, Costarelli S, Morelli G, Tartaglia T. The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infection. BMC Infect Dis 2006;6:54.
19. Faine BA, Harland KK, Porter B, Liang SY, Mohr N. A clinical decision rule identifies risk factors associated with antimicrobial-resistant urinary pathogens in the emergency department: A retrospective validation study. Ann Pharmacother 2015;49:649-55.
20. Bennett WM, Craven R. Urinary tract infections in patients with severe renal disease. Treatment with ampicillin and trimethoprim-sulfamethoxazole. JAMA 1976;236:946-8.