Introduction

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

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 ≥10^5 CFU/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.

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 ≥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
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 ≥10⁵ 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%).

**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...
involved in UTI and this is observed both in the outpatient setting and in hospitalized patients.\textsuperscript{[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 \textit{E. coli} (58.3\%, \textit{n} = 293), followed by \textit{Klebsiella pneumoniae}.\textsuperscript{[1]} Similar findings were also shown in the study of Jadav et al., where \textit{E. coli} was the predominating uropathogen in HD patients,\textsuperscript{[14]} while in the study of Jaiswal et al., \textit{E. coli} was the most common microorganism in male HD patients.\textsuperscript{[15]} D’Agata et al. reported that \textit{Candida} spp. was the most common pathogen implicated in nosocomial UTI in HD patients.\textsuperscript{[16]} Our findings concur with the bulk of existing literature. In addition, we further demonstrate that \textit{E. coli} growth is significantly associated with PKD. Autosomal dominant PKD is responsible for about 5\% of ESRD.\textsuperscript{[17]} Infection of a cyst can occur from bacteremia or the urine in an ascending manner.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[1]} The presence of diabetes mellitus was also reported to have no effect on the types of uropathogens.\textsuperscript{[11,18]} 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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[1,19]}

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Conflicts of interest
There are no conflicts of interest.

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

| Resistant microorganisms                          | Dialysis patients, \textit{n} (%) |
|--------------------------------------------------|----------------------------------|
| \textit{E. coli} ESBL                              | 12 (41.4)                        |
| \textit{E. coli} MDR                              | 1 (3.4)                          |
| \textit{Klebsiella} carabapenemase                 | 2 (6.9)                          |
| VRE                                              | 7 (24.1)                         |
| MRSA                                             | 5 (17.2)                         |
| \textit{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 \textit{Staphylococcus aureus}, \textit{E. coli}: \textit{Escherichia coli}
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