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BRIEF REPORT

Significance of bacteriuria in patients with end-stage renal disease on hemodialysis

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ABSTRACT

The significance of bacteriuria in patients with end-stage renal disease (ESRD) on hemodialysis (HD) is unclear. It is not known whether treatment of asymptomatic bacteriuria is associated with lower rates of urinary tract infection or readmission. Adult patients with ESRD on HD were retrospectively evaluated to assess factors associated with the recurrence of bacteriuria and readmission. We included 68 patients in the analysis. There were 20 patients (29.4%) with urinary symptoms. All symptomatic patients received antibiotic therapy, whereas half of the asymptomatic patients received antibiotics. Antibiotic use was not associated with lower rates of readmission or the recurrence of bacteriuria.

Key words: Dialysis, stewardship, urinary tract infection, urine

INTRODUCTION

Bacteriuria is believed to be a potential reservoir for infections leading to cystitis, pyelonephritis, and perinephric abscess. One in four asymptomatic hemodialysis (HD) patients had bacteriuria in one study.[1] The utility of pyuria and other urine indices are low in predicting bacteriuria in patients with end-stage renal disease (ESRD) making urine culture an important method for the diagnosis of urinary tract infection (UTI) in this population.[2-4] The significance of bacteriuria in patients with ESRD is unclear. The Infectious Diseases Society of America does not recommend treatment of asymptomatic bacteriuria in most patients except in pregnancy and before invasive urologic procedures.[5] However, there are limited data regarding the impact of treatment for asymptomatic bacteriuria in patients with ESRD receiving HD and whether it is associated with lower rates of UTI or readmission rate.

The main aims of this study were as follows: (1) to assess factors associated with recurrence of bacteriuria and readmission in ESRD patients with bacteriuria, and (2) to assess whether antibiotic treatment was associated with lower rates of admission or recurrence.

METHODS

We conducted a retrospective medical records review of patients with ESRD on HD who were admitted to tertiary care, the academic medical center between January 2008 and December 2014. Patients were included if they had bacteriuria (>100 colony-forming unit/mL) within 1 week before admission or during the admission. Patients on continuous renal replacement therapy, HD for acute renal failure, or peritoneal dialysis were not included in the study. Patients were excluded if they met one of the following criteria: <18-year-old, treatment with antibiotics for a different reason other than bacteriuria at the time of admission, the presence of candiduria, polymicrobial bacteriuria (3 or more organisms), history of renal transplantation, or the presence of bacteremia, sepsis, or pyelonephritis.

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We collected the following data: demographics (age, sex, race, and ethnicity), cause of ESRD (hypertension, diabetes, and others), age-adjusted Charlson comorbidity index adjusted for haemodialysis,[6] semi-quantitative urine culture, the presence of pyuria (defined as ≥10 white blood cells (WBC) per high-power field), and antibiotic use. We assessed for the presence of UTI signs and symptoms (fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; acute hematuria; pelvic discomfort; dysuria, urgent or frequent urination, or suprapubic pain or tenderness). Rates of recurrence of bacteriuria, readmission along with secondary outcomes (*Clostridium difficile* colitis and mortality rates) were evaluated for 6 months after index bacteriuria episode.

Association between predictor variables and recurrence of bacteriuria and readmission were independently evaluated using Chi-square test or Fisher's exact test for discrete variables and an independent, two-sample *t*-test assuming equal variances for continuous variables. Independent variables with apparent associations with disease group ($P < 0.10$) were further considered in a multiple logistic regression model. The values of $P < 0.05$ were considered to be significant for the final model.

RESULT

Review process

A total of 68 patients with ESRD on HD who had bacteriuria during admission or within 1 week of admission were included in this study analysis out of 306 patients screened. Reasons for exclusion (238 patients) are shown in Figure 1 with the most common reasons being patients with a history of renal transplant before index bacteriuria or transplant within 6 months after index bacteriuria ($n = 94$).

Demographics and characteristics of patients

The mean age was 59.5 years (standard deviation [SD] + 15.6). A total of 24 patients were males (35.2%) and 29 were Hispanic White (43%). The most common cause of ESRD was diabetes mellitus (61.8%), and the majority of patients (86.8%) had a high age-adjusted Charlson comorbidity index adjusted for HD (≥5).

Clinical, laboratory and antibiotic data

As shown in Table 1, 20 patients (29.4%) had urinary symptoms with suprapubic pain being the most commonly reported symptom (16.2%), followed by fever or rigors (11.8%), altered mental status (4.4%), urinary frequency (2.9%), and flank pain (2.9%).

Sixty-two patients (91.2%) had pyuria (WBC ≥10). The majority of patients (82.4%) had monomicrobial bacteriuria that was caused by lactose fermenting Gram-negative rods (41.2%). Other organisms seen were nonlactose fermenting Gram-negative rods (11.8%), *Enterococcus* spp. (11.8%), *Streptococci* (11.8%), *Staphylococcus aureus* (2.9%), and *Lactobacillus* (2.9%). The remaining 12 patients (17.8%) had two organisms isolated from urine.

As shown in Table 1, 64.7% of the patients received antibiotics including all 20 symptomatic patients and half

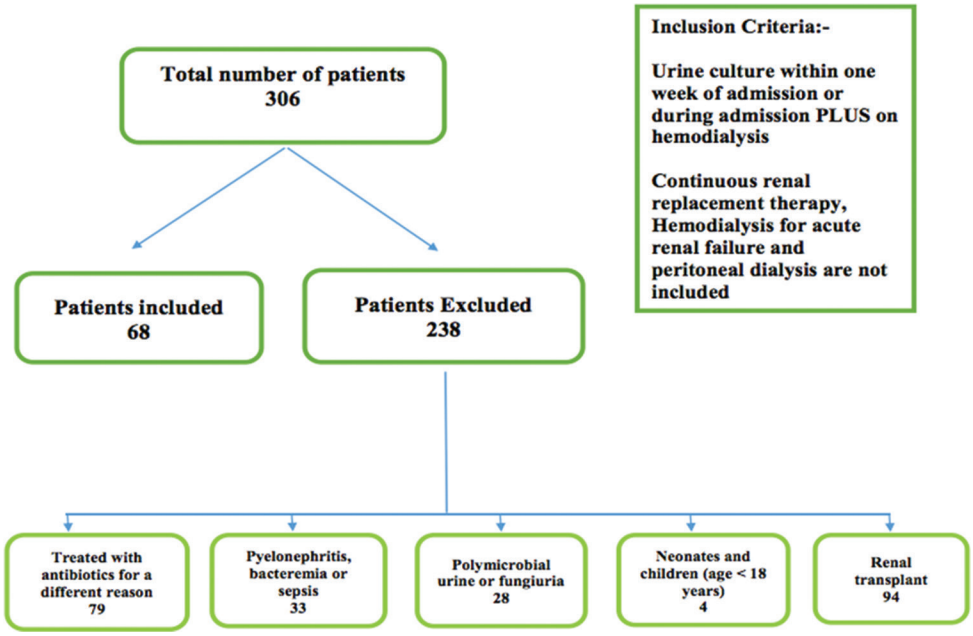

Figure 1: Inclusion criteria are included in the box (top right). Exclusion criteria are shown below

Table 1: Characteristics of patients with end-stage renal disease on hemodialysis with bacteriuria (*n*=68)

Characteristic	*n* (%)
Clinical symptoms	
Symptomatic patients (urinary)	20 (29.4)
Suprapubic pain	11 (16.8)
Dysuria	9 (13.2)
Fever or rigors	8 (11.8)
Altered mental status	3 (4.4)
Frequency	2 (2.9)
Flank pain	2 (2.9)
Laboratory and microbiologic data	
Presence of pyuria (WBC≥10)	62 (91.2)
Urine sample colony count	
$\leq 10^3$	1 (1.5)
10^3-10^4	3 (4.4)
10^4-10^5	30 (44.1)
$\geq 10^5$	34 (50.0)
Patients with only one organism identified from urine cultures	56 (82.4)
Organisms identified in monomicrobial urine cultures	
Lactose fermenter Gram-negative rods	28 (41.2)
Nonlactose fermenter Gram-negative rods	8 (11.8)
Enterococcus sp	8 (11.8)
Streptococci sp	8 (11.8)
Staphylococcus aureus	2 (2.9)
Lactobacillus sp	2 (2.9)
Antibiotics prescribed	
Fluoroquinolone (ciprofloxacin or levofloxacin)	21 (30.9)
Beta-lactams	16 (23.5)
Trimethoprim/sulfamethoxazole	3 (4.4)
Glycopeptide (vancomycin)	3 (4.4)
Nitrofurantoin	1 (1.5)
No antibiotic prescribed	24 (35.3)

WBC: White blood cells

of the asymptomatic patients (n = 24). Fluoroquinolones were the most common class of antibiotic prescribed (30.9% of all study patients), followed by beta-lactams (23.5%).

Recurrence of bacteriuria

A total of 11 patients (16.2%) had a recurrence of bacteriuria within 6 months of the first episode. Independent analysis showed that bacteriuria recurrence among female was significantly higher than in males (25% vs. 0%, $P = 0.006$). Age, race, ethnicity, type of renal disease, the presence of pyuria, symptoms, Charlson index, colony count, and polymicrobial bacteriuria were not associated with bacteriuria recurrence. There was no statistically significant difference in bacteriuria recurrence between patients who received antibiotics compared to those who did not (13.6% vs. 20.8%, $P = 0.5$). Subgroup analysis showed similar results in symptomatic and asymptomatic patients (data not shown).

Readmission

A total of 34 patients (50%) were readmitted within 6 months of index bacteriuria episode. Only one patient was readmitted for urinary symptoms (recurrent dysuria). Independent analysis showed that younger age, race (nonwhite), a renal disease caused by diabetes mellitus, and the absence of pyuria were associated with readmission within 6 months of bacteriuria.

These variables were further analyzed using a multiple logistic regression model, and they remained statically significant ($P < 0.05$). Sex, ethnicity, Charlson index, symptoms, colony count, and polymicrobial bacteriuria were not associated with readmission. In addition, there was no statistically significant difference in readmission between patients who received antibiotics compared to those who did not receive antibiotics (50% vs. 50%, $P = 1$).

Follow-up and secondary outcomes

Forty-eight patients (70.1%) had follow-up for 6 months or more. Mean follow-up duration was 140.5 days (SD + 67.7). Nine patients (13.2%) developed *Clostridium difficile* colitis within 6 months of bacteriuria episode. Two patients died during follow-up on days 132 and 133, respectively, due to ventricular tachycardia. Ten patients developed bacteriuria due to different organisms other than the index case. Independent analysis for association between independent variables (such as antibiotic use and symptoms) and secondary outcomes was not performed due to a small number of patients who developed the secondary outcomes.

DISCUSSION

To the best of our knowledge, this is the first study that assessed the significance of asymptomatic bacteriuria in patients with ESRD. Data from our study showed that most ESRD patients with bacteriuria were asymptomatic (70.6%). There was a low rate of bacteriuria recurrence (16.2%) and readmission due to urinary symptoms (1.5%) within 6 months of index bacteriuria.

More than half of the patients (64.7%) with asymptomatic bacteriuria in our study received antibiotic therapy despite the current guidelines from the Infectious Diseases Society of America.[4] It is possible that healthcare providers were either not aware of these recommendations or they may have felt that they did not apply to patients with ESRD due to different reasons (abnormal immune system or production of only a small amount of urine). One patient received nitrofurantoin that is not recommended in patients with ESRD due to inadequate urinary concentrations.

One important finding from our study was that antibiotic use was not associated with lower rates of readmission

or recurrence of bacteriuria. This supports the recommendations from the Infectious Diseases Society of America regarding not treating patients with asymptomatic bacteriuria in this population. Withholding antibiotics in asymptomatic patients with ESRD on HD with bacteriuria may prevent them from developing *Clostridium difficile* infection, multi-drug resistant organisms, or side effects due to antibiotic use.

The study has several limitations. Over 75% of patients with ESRD were excluded leading to a small number of patients included in the study. The study was retrospective in nature. In addition, it was based on experience at one medical center, which limits the generalizability of our data to other centers.

CONCLUSION

Asymptomatic bacteriuria in patients with ESRD on HD is associated with low rates of recurrence and readmission due to urinary symptoms. There was no association between antibiotic use and recurrence of bacteriuria or readmission. Avoiding antibiotics in asymptomatic patients should be considered.

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Conflicts of interest

There are no conflicts of interest.

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