

# Hospital-Acquired Infections Among Chronic Hemodialysis Patients

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● The epidemiological characteristics of nosocomial infections among patients requiring chronic hemodialysis, a high-risk and rapidly growing population, have not been fully elucidated. During a 30-month cohort study, rates of bloodstream infections (BSIs), urinary tract infections (UTIs), pneumonia, and diarrhea caused by *Clostridium difficile* and the distribution of pathogens among hospitalized chronic hemodialysis patients were compared with hospitalized patients not requiring chronic hemodialysis. To identify risk factors for developing a nosocomial infection among chronic hemodialysis patients, a matched case-control study was performed. A total of 1,557 nosocomial infections were detected during 1,317 of 68,361 admissions (2%). Of these, 47 nosocomial infections occurred in chronic hemodialysis patients during 31 of 578 admissions (5%). Nosocomial infections were significantly more frequent among the chronic hemodialysis group (9.1/1,000 patient-days) compared with the non-chronic hemodialysis group (3.8/1,000 patient-days; relative risk [RR], 2.4; 95% confidence interval [CI], 1.8 to 3.2;  $P < 0.001$ ). UTIs were the most common nosocomial infections among chronic hemodialysis patients, accounting for 47% of all infections in this population. UTIs were significantly more common among chronic hemodialysis patients (4.2/1,000 patient-days) compared with non-chronic hemodialysis patients (0.7/1,000 patient-days; RR, 6.2; 95% CI, 3.8 to 9.5;  $P < 0.001$ ). Among chronic hemodialysis patients, *Candida* spp and enterococci were the most common pathogens in contrast to coagulase-negative staphylococci and *Staphylococcus aureus* among patients not requiring hemodialysis. Using conditional logistic regression, a greater index of comorbidity was significantly associated with nosocomial infections among the chronic hemodialysis population (odds ratio, 3.6; 95% CI, 1.2 to 10.7;  $P = 0.02$ ). Chronic hemodialysis patients are at a substantially greater risk for developing a nosocomial infection compared with other hospitalized patients.

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**INDEX WORDS:** Infection; hemodialysis (HD); risk factors; hospitals; cross-infection; urinary tract infections (UTIs).

**T**HE NUMBER OF patients with end-stage renal disease is increasing by 9% per year.<sup>1</sup> Among those undergoing hemodialysis, the majority will require at least one hospitalization every year.<sup>2</sup> Once hospitalized, these patients have an intrinsic susceptibility to developing an infection as a result of numerous comorbid conditions, uremic toxicity, and anemia of chronic renal failure, all of which contribute to an immunocompromised state.<sup>3-6</sup> In addition, chronic hemodialysis patients depend on vascular access, which increases the risk for developing bacteremia, the nosocomial infection with the greatest mortality rate.<sup>7</sup>

Nosocomial infections contribute directly to a substantial number of hospital deaths and extra hospital days.<sup>7</sup> These infections have not been extensively investigated in chronic hemodialysis patients, even though they are a high-risk population. To develop effective and customized prevention strategies, the epidemiological characteristics of nosocomial infections need to be fully elucidated in this population.

To determine the incidence of nosocomial infections and survey the causative pathogens, a 30-month prospective surveillance study was performed on all hospitalized chronic hemodialysis patients admitted to a tertiary-care medical center. Results among chronic hemodialysis patients

were compared with those of patients not undergoing hemodialysis who were hospitalized during the same time. In addition, to identify risk factors for nosocomial infections among chronic hemodialysis patients, a matched case-control study was performed.

## METHODS

### Patient Population

The Vanderbilt University Medical Center (Nashville, TN) is a 663-bed tertiary-care hospital with an average of 28,000 patient discharges per year. During July 1, 1995, through December 31, 1997, hospital-wide surveillance for nosocomial infections was performed. Patients undergoing hemodialysis during their hospitalization were identified by reviewing billing records with specific Current Procedural Terminology codes for hemodialysis (codes 90935 and

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90937). Demographic and clinical data were obtained by reviewing computerized medical records. Chronic renal failure was defined as hemodialysis initiated before the current hospital admission. Comorbid conditions were assessed by the Charlson index.<sup>8</sup> Patients were classified as immunocompromised if they were administered immunosuppressive medications or had human immunodeficiency virus infection or a malignancy.

### Surveillance of Hospital-Acquired Infections

During the study period, trained, experienced infection control nurses performed prospective hospital-wide nosocomial infection surveillance according to the standard protocol of the National Nosocomial Infection Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC).<sup>9</sup> Daily lists of patients with positive culture results from any site were obtained from the clinical microbiology laboratory. Medical charts of these patients were reviewed to determine if a positive culture result represented contamination, colonization, or an infection. A nosocomial infection was defined as an infection not present or incubating at the time of hospital admission. Definitions established by the NNIS system for site-specific nosocomial infections were used.<sup>9</sup>

The four most common nosocomial infections occurring among nonsurgical patients were evaluated in this study: pneumonia, primary bloodstream infections (BSIs), urinary tract infections (UTIs), and diarrhea caused by *Clostridium difficile* (CD). According to the NNIS criteria, primary BSIs included those infections related to an intravascular device. For each documented UTI, urinary catheterization or other instrumentation of the urinary tract during the prior 7 days was recorded. Nosocomial infection rates among patients undergoing chronic hemodialysis were compared with rates among patients hospitalized during the same study period who were not undergoing hemodialysis. Identification of pathogens was performed by the clinical microbiology laboratory, following the guidelines of the National Committee for Clinical Laboratory Standards.<sup>10</sup>

### Case-Control Study

To define the risk factors for developing a nosocomial infection among the cohort of chronic hemodialysis patients, a matched case-control study was performed. Cases were defined as all chronic hemodialysis patients who developed a nosocomial infection during the study period; controls were selected from chronic hemodialysis patients who did not develop a nosocomial infection. For those patients admitted more than once during the study period, only the earliest admission was included in the analysis. One control was selected for each case. Matching criteria included year of hospital admission and duration of hospitalization.

### Statistical Analysis

Categorical variables were compared using chi-square or Fischer's exact test. Continuous variables were compared using Student's *t*-test or Wilcoxon's rank-sum test for nonparametric distributions. Conditional logistic regression was used to estimate the odds ratio of potential risk factors for developing a nosocomial infection among the matched cases

and controls. A *P* value of 0.05 or less was considered statistically significant. All analyses were performed using Stata 6.0 (Stata Corporation, College Station, TX).

## RESULTS

### Hospital-Acquired Infections

During the 30-month study period, there were 68,361 patient admissions to the hospital. Of these, 365 patients required chronic hemodialysis during 578 admissions. These chronic hemodialysis patients had a mean age of  $55 \pm 8$  (SD) years. Fifty-two percent were men, 56% were Caucasian, and 43% had diabetes mellitus. The most common underlying causes of kidney disease were diabetes mellitus (41%) and hypertension (31%).

A total of 1,557 nosocomial infections (pneumonia, BSIs, UTIs, and CD) were detected throughout the hospital. These nosocomial infections occurred during 1,317 (2%) patient admissions. Among these, 47 nosocomial infections occurred during 31 admissions (5%) requiring chronic hemodialysis. Thus, nosocomial infections occurred significantly more frequently during admissions that required chronic hemodialysis (31 of 578 admissions) than during admissions that did not require hemodialysis (1,286 of 67,783 admissions; relative risk [RR] 2.9; 95% confidence interval [CI], 2 to 4;  $P < 0.001$ ).

Among patients undergoing chronic hemodialysis, the median length of stay was 25 days (range, 9 to 96 days) for those patients who developed a nosocomial infection compared with a median of 4 days (range, 1 to 76 days) for those chronic hemodialysis patients who did not develop a nosocomial infection ( $P < 0.001$ ). Hospital wide, the median length of stay for all patients was 5 days. Even after adjusting for total length of hospital stay, nosocomial infections were significantly more frequent among patients undergoing chronic hemodialysis (9.1/1,000 patient-days) than among patients who did not require chronic hemodialysis (3.8/1,000 patient-days; RR, 2.4; 95% CI, 1.8 to 3.2;  $P < 0.001$ ).

The specific types of nosocomial infections according to chronic hemodialysis exposure are listed in Table 1. Nosocomial UTIs were the most common nosocomial infection among the chronic hemodialysis population, accounting for nearly half the nosocomial infections (47%). Notably, all 22 nosocomial UTIs in the chronic

**Table 1. Nosocomial Infection Rates According to Chronic Hemodialysis Exposure**

Type	No. of Infections (%)		Per 1,000 Patient-Days		RR (95% CI)	P
	CHD (n = 47)	Non-CHD (n = 1,510)	CHD (n = 5,182)	Non-CHD (n = 398,983)		
Urinary tract infection	22 (47)	275 (18)	4.2	0.7	6.2 (3.8-9.5)	<0.001
Bloodstream infection	13 (28)	558 (37)	2.5	1.4	1.8 (1.1-3.1)	0.05
Pneumonia	9 (19)	612 (41)	1.7	1.5	1.1 (0.5-2.2)	0.7
<i>Clostridium difficile</i> diarrhea	3 (6)	65 (4)	0.6	0.2	3.6 (0.7-11)	0.07

Abbreviation: CHD, chronic hemodialysis.

hemodialysis patients were symptomatic with fever and urinary tract symptoms. Instrumentation of the urinary tract occurred among 20 chronic hemodialysis patients with UTI (91%), of whom 17 patients had an indwelling urinary catheter during the prior 7 days. There was no significant difference in the frequency of instrumentation of the urinary tract among the chronic hemodialysis patients with UTIs (20 of 22 patients) compared with nonhemodialysis patients with UTIs (237 of 275 patients;  $P = 0.5$ ).

Among the non-chronic hemodialysis population, pneumonia was the most common nosocomial infection (41%). BSIs were the second most frequent nosocomial infection in both the chronic hemodialysis and non-chronic hemodialysis groups. Of the 13 BSIs among chronic hemodialysis patients, 1 BSI was associated with an arteriovenous fistula infection and 4 BSIs were associated with temporary central catheter infections. CD was the least frequent nosocomial infection in both groups.

After adjusting for length of hospital stay, UTIs and BSIs were significantly more frequent among the chronic hemodialysis group compared with the nonhemodialysis group. There was a trend toward a greater rate of CD diarrhea among chronic hemodialysis patients compared with nonhemodialysis patients after adjusting for length of hospital stay ( $P = 0.07$ ; Table 1).

#### Distribution of Nosocomial Pathogens

The most frequent bacterial pathogens recovered from nosocomial infections (UTIs, BSIs, pneumonia) according to hemodialysis exposure are listed in Table 2. Chronic hemodialysis patients had a different distribution of bacterial pathogens implicated in nosocomial infections compared with patients not requiring hemodialy-

sis. Among patients undergoing chronic hemodialysis, enterococci and *Candida* spp were the most common pathogens compared with coagulase-negative staphylococci and *Staphylococcus aureus* among patients not requiring hemodialysis.

#### Infections Occurring in the Intensive Care Unit

The proportion of nosocomial infections occurring while patients were in the intensive care unit (ICU) was significantly less among patients undergoing chronic hemodialysis (22 of 47 patients) compared with patients not requiring hemodialysis (1,020 of 1,510 patients; RR, 0.4; 95% CI, 0.2 to 0.7;  $P = 0.003$ ). BSIs and CD occurred in the ICU significantly more often among the nonhemodialysis group compared with the chronic hemodialysis group ( $P = 0.03$ ; Fig 1).

The frequency of pathogens implicated in ICU infections was analyzed for the four most common pathogens isolated from the chronic hemodialysis group. Infections caused by *Enterobacter* spp occurred more frequently and *Pseudomonas aeruginosa* infections less frequently in the ICU among the chronic hemodialysis group compared with the nonhemodialysis group ( $P < 0.05$ ). There was no statistically significant difference in the frequency of enterococcal or candidal infections occurring in the ICU between the two groups (Fig 2).

#### Case-Control Study

Twenty-nine patients during 31 admissions requiring chronic hemodialysis developed at least one nosocomial infection. These patients were matched to 29 chronic hemodialysis patients who did not develop a nosocomial infection. All cases were matched to controls by year of admission. Cases were also matched to controls by

**Table 2. Distribution of Most Common Bacterial Pathogens Isolated From Nosocomial Infections According to Hemodialysis Exposure**

Pathogen	Type of Infection (%)							
	No. of Pathogens (%)*		Urinary Tract Infections		Bloodstream Infections		Pneumonia†	
	CHD (n = 48)	Non-CHD (n = 1,702)	CHD (n = 22)	Non-CHD (n = 314)	CHD (n = 13)	Non-CHD (n = 661)	CHD (n = 5)	Non-CHD (n = 412)
<i>Enterococcus</i> spp	6 (13)	144 (8)	2 (9)	46 (15)	4 (31)	98 (15)	0 (0)	0 (0)
<i>Candida</i> spp	8 (17)	90 (5)	6 (27)	42 (13)	2 (15)	48 (7)	0 (0)	59 (14)
<i>Enterobacter</i> spp	6 (13)	79 (5)	3 (14)	15 (5)	2 (15)	18 (3)	1 (20)	46 (8)
<i>Pseudomonas aeruginosa</i>	5 (10)	174 (10)	4 (18)	43 (14)	1 (8)	15 (2)	0 (0)	116 (19)
<i>Staphylococcus aureus</i>	3 (6)	201 (12)	0 (0)	8 (3)	1 (8)	65 (10)	2 (40)	128 (21)
<i>Escherichia coli</i>	3 (6)	107 (6)	3 (14)	69 (22)	0 (0)	17 (3)	0 (0)	21 (3)
Coagulase-negative staphylococci	1 (2)	245 (14)	0 (0)	4 (1)	1 (8)	241 (36)	0 (0)	0 (0)
Other‡	16 (33)	662 (39)	4 (18)	87 (28)	2 (15)	159 (24)	2 (40)	42 (10)

Abbreviation: CHD, chronic hemodialysis.

\*More than one pathogen isolated per infection.

†Pathogen not identified in all cases.

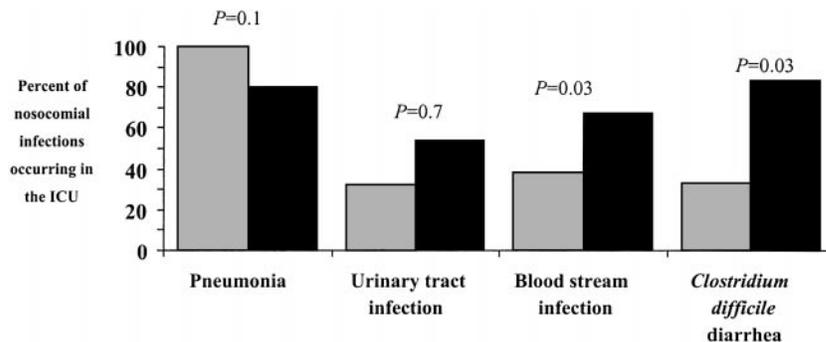
‡Two organisms or less per species in the CHD group, including *Morganella* spp, *Klebsiella* spp, *Stenotrophomonas* spp, *Acinetobacter* spp, *Citrobacter* spp, *Proteus* spp, *Aeromonas* spp, *Streptococcus* spp, and *Aspergillus* spp.

total duration of hospitalization: 26 cases within 1 day and 3 cases, who remained in the hospital greater than 40 days, within 6 days.

Using conditional logistic regression, chronic hemodialysis patients who developed a nosocomial infection had a significantly greater index of comorbidity, as defined by the Charlson score (Table 3). There were no differences in patient demographic characteristics, presence of diabetes mellitus, or an immunocompromised state. Five patients (17%) among the cases died and one patient (3%) among the controls died (odds ratio, 5.0; 95% CI, 0.6 to 43;  $P = 0.1$ ).

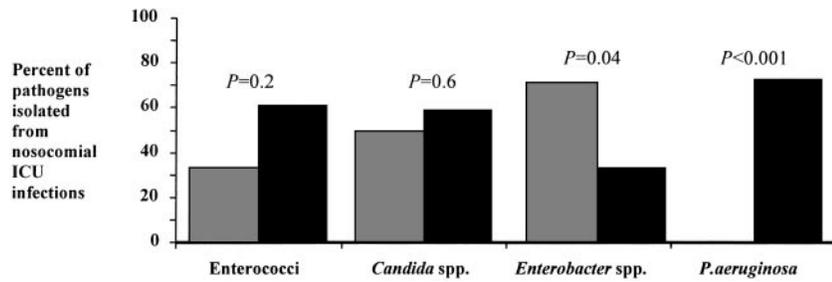
## DISCUSSION

A 30-month prospective cohort study was performed to describe the epidemiological characteristics of four of the most common nosocomial infections, pneumonia, BSIs, UTIs, and CD, among chronic hemodialysis patients. The results of this study show that patients undergoing chronic hemodialysis were at a significantly greater risk for developing a nosocomial infection compared with patients not requiring chronic hemodialysis and that these infections occurred more commonly outside of the ICU setting among



**Fig 1. Proportion of nosocomial infections occurring in the ICU according to chronic hemodialysis exposure. (□) Chronic hemodialysis; (■) non-chronic hemodialysis.**

**Fig 2. Proportion of bacterial pathogens implicated in nosocomial ICU infections according to chronic hemodialysis exposure.** (□) Chronic hemodialysis; (■) non-chronic hemodialysis.



chronic hemodialysis patients. A greater index of comorbidity among the chronic hemodialysis population was associated with a 3.6-fold increased risk for developing a nosocomial infection, even after matching for the confounding effects of year of hospital admission and duration of hospitalization.

Chronic hemodialysis patients had a distinctive distribution of nosocomial pathogens. The NNIS system of the CDC has consistently reported coagulase-negative staphylococci and *Escherichia coli* as the major pathogens implicated in BSIs and UTIs, respectively. These findings are in agreement with the nosocomial infections detected among the nonhemodialysis population in this study. In contrast, among the chronic hemodialysis population in this study, enterococci and *Candida* spp were the pathogens most commonly associated with BSIs and UTIs, respectively. With the rapidly increasing rates of vancomycin-resistant enterococci in the dialysis

population and the limited therapeutic options for the treatment of these infections,<sup>11</sup> the predominance of enterococci implicated in nosocomial BSIs in this population is concerning. Furthermore, among all types of nosocomial infections, bacteremias are associated with the greatest mortality.<sup>7</sup> Thus, the potential for greater mortality rates from nosocomial bacteremias in the dialysis population needs to be considered. Likewise, the predominance of *Candida* spp as the causative pathogens for nosocomial UTIs suggests that these infections may be associated with greater morbidity and mortality among hemodialysis patients compared with other hospitalized patients in whom gram-negative pathogens predominate.<sup>7,12,13</sup> The outcome of nosocomial infections among chronic hemodialysis patients warrants further elucidation.

The urinary tract may not be recognized as an important source of infection among the chronic hemodialysis population in view of the minimal urine output in these patients. The results of this study imply otherwise. Symptomatic UTIs were the most common nosocomial infections among the chronic hemodialysis patients. The diagnosis of UTI was based on strict CDC criteria, including the recovery of a single pathogen in concentrations greater than 10<sup>5</sup> colonies per milliliter from a urine specimen, in addition to urinary tract symptoms or fever without another source. Therefore, positive urine culture results were unlikely to represent bacterial overgrowth in residual bladder urine.

These results suggest that the urinary tract is an important source of fever and infection among hospitalized chronic hemodialysis patients with urine output. In this study, the majority of hemo-

**Table 3. Risk Factors for Nosocomial Infections Among Hospitalized Patients Requiring Chronic Hemodialysis**

Characteristic	Cases (n = 29)	Controls (n = 29)	OR (95% CI)	P
Mean Charlson score	4.2	2.8	3.6 (1.2-10.7)	0.02
Age* (y)	55 ± 4	52 ± 3	1.0 (0.9-1.1)	0.3
Sex (men/women)	11/18	7/22	1.4 (0.4-4.4)	0.6
Diabetes mellitus	10	6	2.0 (0.6-6.4)	0.2
Immunocompromised state	5	9	0.4 (0.1-1.7)	0.2

Abbreviation: OR, odds ratio.  
\*Mean ± SD.

