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# A Retrospective Quality Study of Hemodialysis Catheter-Related Bacteremia in a Danish Hospital

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## Abstract

**Background:** Hemodialysis catheter-related bacteremia (HD CRB) is a major complication of long-term hemodialysis (HD) therapy and bacteremia is secondary only to cardiovascular disease as the leading cause of death in patients receiving renal replacement therapy. A large part may be preventable and surveillance is a critical aspect of infection control and prevention. **Aim:** To analyze incidence, causative species, and treatment of HD CRB in adult chronic HD patients at Nordsjaellands Hospital (NOH), Denmark. **Methods:** All episodes of bacteremia in the Department of Cardiology, Nephrology and Endocrinology (KNEA), NOH from 2010 to 2013 were analyzed. **Inclusion criteria:** Adult chronic HD patients with a tunneled dialysis catheter diagnosed with HD CRB. Causative microorganism and antimicrobial treatment were recorded for each episode. **Findings:** Ninety-nine episodes of HD CRB in 72 patients were found with a mean incidence rate of 0.9/1000 catheter-days. Gram-positive bacteria were isolated in 71% of the episodes, gram-negative bacteria in 25%, both in 3%, and yeast in 1%. The most frequently isolated microorganisms were *Staphylococcus aureus* (33%), Coagulase-negative staphylococci (29%), enterobacteriaceae (20%) and enterococci (8%). The most commonly used empiric antimicrobials were cefuroxime and vancomycin and the overall efficacy was 77%. **Conclusion:** The well-functioning infection prevention strategy seems to be successful resulting in a relatively low incidence rate of HD CRB compared with that shown in international studies. The high proportion of gram-negative bacteria raises the question as to whether future antimicrobial guidelines should cover both gram-positive and gram-negative bacteria.

## Keywords

Hemodialysis, Bacteremia, Microbiology, Surveillance, Quality Improvement

## 1. Introduction

Bacteremia is a serious condition associated with substantial morbidity and a high short-term mortality rate [1] [2] [3] [4]. In Denmark, about 35% of the bacteremic episodes are nosocomial and approximately 20% are health-care acquired (patients with a hospital stay in the 30 days before hospital admission or who have regular hospital visits (e.g. for hemodialysis (HD) or chemotherapy)) [3]. This means that a large part of this serious problem may be preventable; consequently, focus on establishing an effective infection prevention strategy is paramount.

Patients with end-stage renal disease receiving chronic HD through a central venous catheter (CVC) are more susceptible to bacteremia than others, due to the direct access to the bloodstream, several comorbidities and an impaired immune system.

In 2013 approximately 2000 patients received chronic HD treatment in Denmark [5]. International studies have shown that the incidence rate of HD catheter-related bloodstream infections (CRBSI) is between 0.45 and 5.5 episodes per 1000 catheter-days and the hazard ratio for bacteremia in patients with tunneled CVCs compared with patients with native arterio-venous (AV) fistulas is approximately 5 [6]-[11].

Interventions proven to be effective in reducing the incidence rate of catheter-related bacteremia in HD patients are: surveillance, good hand hygiene, hygiene audits, aseptic techniques, staff and patient education, and reduction in the number of HD catheters [12] [13] [14].

Nevertheless, it is estimated that almost 30% of HD patients depend on CVCs as their primary vascular access and for some of these patients the use of HD catheters is unavoidable [13] [15].

The aim of this study was to analyze incidence, causative species, and treatment of hemodialysis catheter-related bacteremia (HD CRB) in adult chronic HD patients at Nordsjaellands Hospital (NOH), Denmark from 2010-2013.

## 2. Methods

### 2.1. Study Design

A single center, retrospective, quality study performed on adult chronic HD patients diagnosed with HD CRB in Department of Cardiology, Nephrology and Endocrinology (KNEA), NOH from 2010 to 2013.

Approximately 150 patients at NOH are on chronic HD treatment and approximately 40% have a tunneled CVC [5].

### 2.2. Study Population

All cases of bacteremia in KNEA, NOH from 2010-2013 were screened by reviewing the unitary electronic health records (EHR). Eligible patients were aged  $\geq 18$  years, on chronic HD through a tunneled CVC and diagnosed with HD CRB in the study period. Patients receiving HD through another type of vascular access or with other sources of infection were excluded.

### 2.3. Data Collection

The EHR of the identified patients were reviewed by a nephrologist at NOH and clinical and demographic variables were recorded in a database. The following variables were collected: civil registration number [16], age, name, sex, vascular access type (HD catheter/AV fistula/graft), catheter type (permanent/acute), date of positive blood sample collection, location of blood sample collection, and type of microorganism isolated.

Department of Clinical Microbiology, Herlev and Gentofte Hospital, University of Copenhagen, routinely identified the microorganisms cultured from blood and performed antibiotic susceptibility testing. The antibiograms were retrospectively retrieved and analyzed in December 2014.

Information on the antimicrobial treatment was retrieved from the EHR, which include an electronic medication module. Antimicrobial treatment was analyzed in relation to the antibiograms of the microorganisms isolated from blood cultures.

### 2.4. Study Definitions

A chronic HD patient was defined as a patient on HD through a tunneled permanent CVC. A blood culture typically includes four vials taken from the catheter and/or four vials taken from a peripheral vein (two aerobe and two anaerobe, respectively).

An episode of HD CRB was defined as a positive blood culture with a bacterial or fungal isolate taken from the CVC or a peripheral vein of a patient on chronic HD therapy with no other identified source of infection. An episode was considered polymicrobial if more than one microorganism was isolated from the blood on the same date. Two episodes of HD CRB in the same patient were defined as two separate positive blood cultures with different microorganisms taken at intervals of more than 24 hours or two positive blood cultures with the same isolated microorganism taken at an interval of more than 28 days.

The empiric antimicrobials were defined as all antimicrobials given before knowing the species of the isolated microorganisms. The empiric treatment was considered effective if all bacteria/fungi cultured from the blood were susceptible to one or more of the given empiric antimicrobials.

All episodes were considered as health-care associated infections (HCAI) according to the definition from Friedman *et al.* and the European Centre for Disease Prevention and Control (ECDC) [17] [18].

### 2.5. Outcome

The outcomes of the study were the incidence rate of HD CRB per 1000 catheter-days, the frequencies of the different bacterial/fungal isolates and the efficacy of the empiric antimicrobials.

### 2.6. Statistical Analysis

The incidence rate of HD CRB per 1000 catheter-days was calculated for each quarter in the four-year study period.

Catheter-days is an estimate found by counting the number of tunneled catheters in use per quarter and multiplying it by the number of days in the quarter.

Data are presented as median, range and interquartile range (IQR). Frequency distribution is presented as histograms and a pie diagram. Fisher's exact test was used for comparison of microbial isolates in men and women,  $p < 0.05$  was considered significant.

## 2.7. Ethics

The study was approved by the Regional Scientific Ethics Committee (H-2-2014-FSP-73).

## 3. Results

### 3.1. Patient Characteristics

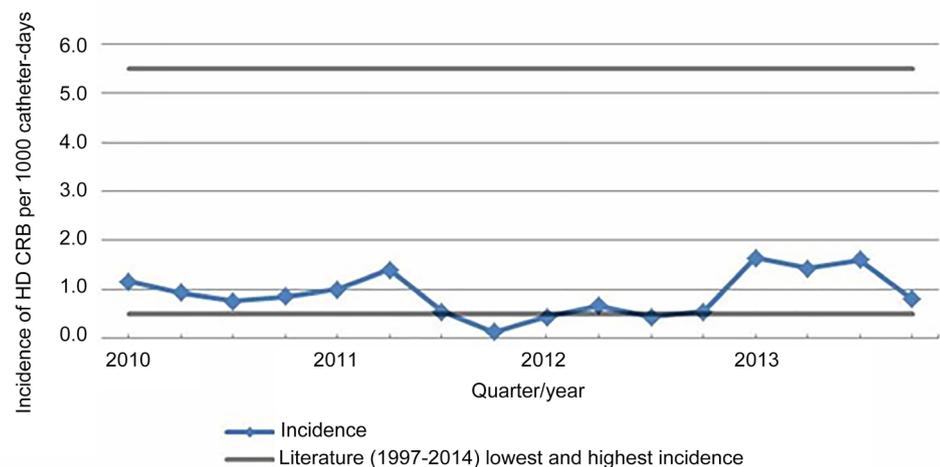
We identified 72 patients with HD CRB; 48 (67%) were male and the patients had a median age of 66 years (IQR 52 - 71 years). Of those identified, 55 (76%) had one episode of HD CRB in the study period, 10 (14%) had two episodes, five (7%) had three episodes and two (3%) had more than three episodes (one patient had four and one patient had five episodes).

### 3.2. Incidence Rates

The mean incidence rate of HD CRB was 0.9 episodes/1000 catheter-days (range: 0.1 - 1.6). The incidence rate was stable during the study period with the lowest incidence rate found in the fourth quarter of 2011 (0.1) and the highest incidence rate found in the first and third quarter of 2013 (1.6) (**Figure 1**, **Table 1**).

### 3.3. Microbiology and Antibiograms

During the study period, 99 episodes of HD CRB were found of which five (5%) were



**Figure 1.** Incidence rate of HD CRB in adult chronic HD patients, at Nordsjaellands Hospital compared with international studies [6] [7] [8] [9] The incidence rate of HD CRB episodes is shown per 1000 catheter-days for every quarter in the surveillance period (2010-2013).

**Table 1.** The calculated incidence (the number of HD CRB episodes per 1000 catheter-days) per quarter and per year in the study period.

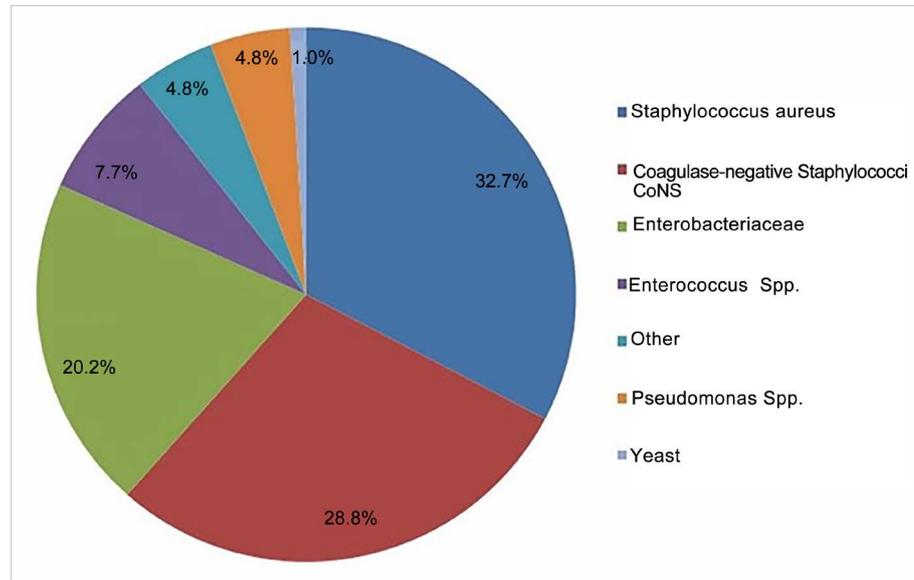
Year	Quarter	Episodes	Catheter-days	Incidence
2010	1	10	8550	1.2
	2	8	8554	0.9
	3	6	7912	0.8
	4	7	8188	0.9
			31	33,204
2011	1	7	7020	1.0
	2	10	7150	1.4
	3	4	7380	0.5
	4	1	7380	0.1
			22	28,930
2012	1	4	8918	0.4
	2	6	8918	0.7
	3	4	9016	0.4
	4	5	9016	0.6
			19	35,868
2013	1	8	4860	1.6
	2	7	4914	1.4
	3	8	4968	1.6
	4	4	4968	0.8
			27	19,710

polymicrobial. We found 104 bacterial/fungal isolates (103 bacterial, 1 fungal). Among the 99 episodes of HD CRB, 70 (71%) were caused by gram-positive bacteria, 25 (25%) were caused by gram-negative bacteria, three (3%) were caused by both gram-positive and gram-negative bacteria and one episode (1%) was caused by yeast (*Candida tropicalis*).

The most frequently isolated microorganisms were *Staphylococcus aureus* (33%), Coagulase-negative staphylococci (CoNS; 29%), and *Enterobacter cloacae* (8%) (Figure 2).

No significant difference in microbial isolates between men and women was observed (Data not shown).

Antibiograms for 92 (93%) episodes could be retrieved. No methicillin-resistant *Staphylococcus aureus* (MRSA), extended spectrum beta-lactamase (ESBL)—producing bacteria, Carbapenemase producing organisms (CPO) or vancomycin-resistant enterococcus (VRE) were found.



**Figure 2.** Distribution (%) of microorganisms responsible for episodes of HD CRB in adult chronic HD patients, at Nordsjaellands Hospital from 2010-2013. A total of 99 episodes of HD CRB occurred in the four-year study period with 104 isolated microorganisms. Coagulase-negative staphylococci; CoNS: *Staphylococcus epidermidis* (17.3%), unspecified CoNS (8.7%), *Staphylococcus hominis* (1%), *Staphylococcus capitis* (1%), and *Staphylococcus lugdunensis* (1%). Enterobacteriaceae: *Enterobacter cloacae* (7.7%), *Escherichia coli* (5.8%), *Aeromonas caviae* (1.9%), *Klebsiella pneumoniae* (1%), *Klebsiella oxytoca* (1%), and *Citrobacter koseri* (1%). *Enterococcus* Spp.: *Enterococcus faecalis* (4.8%), and *Enterococcus faecium* (2.9%). Other: *Streptococcus mitis* (1.9%), *Agrobacterium* species (1%), *Bacteroides fragilis* (1%), and *Micrococcus luteus* (1%). *Pseudomonas* Spp: *Pseudomonas aeruginosa* (2.9%), and *Stenotrophomonas maltophilia* (1.9%). Yeast: *Candida tropicalis* (1%).

### 3.4. Empiric Antimicrobials

Empiric antimicrobials were given in 77 episodes (78%) and the overall efficacy was 77%. Fourteen types of empiric antimicrobials from seven different classes (penicillins, cephalosporins, macrolides, glycopeptides, quinolones, carbapenems, and others (fluconazole and metronidazole)) were used in the study period; the most frequently used were cefuroxime (35 episodes) and vancomycin (27 episodes) (Table 2).

Two or more types of empiric antimicrobials were administered in 44 (44%) episodes.

## 4. Discussion

In the present retrospective quality study of bacteremia in chronic HD patients, the mean incidence rate of HD CRB at NOH was 0.9 episodes/1000 catheter-days, which is low compared with that found in international studies [6] [7] [8] [9] [19]. Due to differences in methods and definitions, several international studies are not directly comparable with the present study. Some studies have investigated the incidence of HD CRB in dialysis patients with all types of CVCs, e.g. the acute single lumen catheters

**Table 2.** List of the types of empiric antimicrobials used and the number of episodes they were used in.

Empiric Antimicrobials (Type)	Count
Cefuroxime	35
Vancomycin	27
Ciprofloxacin	18
Dicloxacillin	14
Meropenem	8
Metronidazole	6
Penicillin	6
Gentamycin	5
Amoxicillin/Clavulanate	3
Flucloxacillin	2
Piperacillin/Tazobactam	2
Cephalexin	1
Fluconazole	1
Roxithromycin	1

[19], while others have defined an HD CRB differently due to differences in national guidelines, different equipment or different means of data collection. Furthermore, many studies calculate the incidence in episodes per person-days or years, which cannot be directly converted to the catheter-days, as used in the present study.

One study, from 2014 in North America by Rosenblum *et al.* [19], reported a bloodstream infection (BSI) rate of 0.81/1000 catheter-days in a catheter hygiene intervention group and a BSI rate of 1.04/1000 catheter-days in their matched control group. Rosenblum *et al.* defined two separate BSIs as two positive blood cultures with 21 days between blood draws, whereas the present study defined it as two positive blood cultures with 28 days between the draws. In another study from North America in 2014 by Moore *et al.* [6], the incidence of CRBSI in all dialysis patients with a tunneled cuffed catheter was reported to be 0.45/1000 catheter-days for a patient group treated with an antibiotic lock solution versus 1.68/1000 catheter-days for the same group treated with the standard heparin lock. The study defined a CRBSI according to criteria established by the Centers for Disease Control and Prevention (CDC), which is in accordance with the definition used in the present study.

The incidence rate in the present study was continuously low during the four-year study period, but reached a maximum in the first and third quarter of 2013 (Figure 1, Table 1). This small increase in incidence rate could be explained by a remarkably low number of catheter-days in 2013 compared with the other three years in the study period (Table 1). The low number could be due to a change in the hospital's geographical up-take area in 2012, which reduced the number of HD patients at NOH.

The most frequently isolated microorganisms in both men and women were Staphy-

lococcus aureus and CoNS, which is in accordance with other studies [6] [9] [20] [21].

An unexpected finding was the relatively high prevalence of bacteremic episodes caused by gram-negative bacteria (27%). However, the results of this surveillance program largely follow those of recent studies [4] [8] [11] [20]. Alexandraki *et al.* investigated the five-year pattern of microorganisms causing bacteraemias in HD patients with an HD catheter and found a significant increase in the incidence of single gram-negative organisms and polymicrobial bacteremia [21]. This trend might be due to an increasing degree of immunodeficiency in the dialysis patients or a failed empiric antibiotic policy, which focuses only on treating the expected gram-positive microorganisms.

During the surveillance period, the most frequently used empiric antimicrobials were cefuroxime and vancomycin, with an overall empiric treatment efficacy of 77%. Notably, cefuroxime was recommended as the empiric antibiotic treatment of sepsis without known focus at NOH in the study period. The recommendation was changed in 2014.

In a recent Danish study of bacteremia by Boel *et al.* [22], an efficacy of empirical antimicrobial treatment of minimum 90% was suggested as acceptable; however, this study differed significantly from the present study as it comprised mostly community-acquired infections and only few patients with an HD catheter. Accordingly, we consider an efficacy of empiric antimicrobials of 77% as acceptable.

In contrast to several other studies, we did not find any MRSA, ESBL-producing bacteria, CPO or VRE [6] [9] [20] [21] [23]. In general, Denmark has a low level of antibiotic resistance compared with many other countries [24].

A well-organized prevention program including surveillance as well as engaging patients and staff in preventive strategies has been reported to have a pronounced beneficial effect on the incidence of infections in dialysis units [25] [26] [27] [28] [29]. The relatively low average incidence rate of HD CRB found in this study is probably a result of the extensive prevention bundle approach found at NOH, consisting of a surveillance program, a vascular access group where dialysis nurses and nephrologists have a special focus on establishing the optimal vascular access for every HD patient, hand hygiene education and audits for both staff and patients and a special no-touch method developed in the daily work with the dialysis patients where no hands or gloves are in direct contact with the head of the dialysis catheter when connecting and disconnecting to the dialysis machine.

Compared with the recommendations from the CDC [14], the infection prevention strategy at NOH follows eight of the nine recommendations.

The ninth recommendation regarding application of antimicrobial ointment to the catheter exit-site during dressing changes is not a part of the local guidelines.

This study is retrospective and observational in nature and therefore has its limitations. 1) Due to the observational nature of the study, there is a risk of selection bias. 2) It is not always possible to definitively determine the source of a bacteremia from electronic patient records when a clinical examination of the patient cannot be performed. 3) There may have been patients with HD CRB hospitalized outside the Department of

Cardiology, Nephrology and Endocrinology, NOH and thereby not included in this study, but it is considered to be a very few patients, if any.

The strength of this study is that monitoring of CRB using the benefits of the Danish Civil Registration System has been routine for several years in the department, which makes the data, albeit retrospective, very robust.

## 5. Conclusion

In conclusion, the NOH infection prevention strategy seems to be successful resulting in a relatively low incidence rate of hemodialysis catheter-related bacteremia during the study period 2010-2013. The unexpected high proportion of gram-negative bacteria, however, raises the question as to whether future antimicrobial guidelines ought to cover both gram-positive and gram-negative bacteria.

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