Patients in Long-Term Care Facilities: A Reservoir for Vancomycin-Resistant Enterococci

Marnie L. Elizaga, Robert A. Weinstein, and Mary K. Hayden

A prospective cohort study with culture surveys and chart reviews was conducted to determine the prevalence of rectal colonization with vancomycin-resistant enterococci (VRE) and to identify risk factors for colonization among 100 residents of 20 different long-term care facilities (LTCFs) who were admitted to 2 medical wards of an academic acute care hospital. On admission to the hospital, 45 (45%) of these 100 patients were determined to be harboring VRE. Prior use of antibiotics and the presence of a decubitus ulcer were identified as risk factors. Fourteen other LTCF residents—33% of those at risk—acquired VRE in the hospital. Antecubital skin colonization with VRE was detected in 28% of patients. Hospital ward surveillance revealed a 60% mean point prevalence of VRE colonization among patients in LTCFs, compared with 21% for other patients (P < .001). Patients in LTCFs in urban referral hospitals are a major reservoir for VRE, which can be transmitted to other inpatients in the hospital, in the LTCF, and in smaller community hospitals.

During the past decade, vancomycin-resistant enterococci (VRE) have become established nosocomial pathogens in intensive care units and, increasingly, on hospital wards. Few options for treatment of VRE infections exist, and concerns about the spread of glycopeptide resistance to other gram-positive bacteria, such as staphylococci, add a special urgency to the VRE problem. Colonization with VRE has been reported from community settings in the United States, including, to a limited degree, long-term care facilities (LTCFs) [1, 2]. However, because of heavy patient traffic between hospitals and LTCFs, we became concerned that foci of colonization with VRE could develop within community-based LTCFs.

Residents of LTCFs are at risk for colonization with drug-resistant gram-negative bacteria, methicillin-resistant Staphylococcus aureus, and enterococci that are resistant to high levels of aminoglycosides; high rates of such colonization have been found [3, 4]. In addition, risk factors for colonization or infection with VRE, such as debilitating diseases and receipt of multiple antibiotics, are widespread among patients in LTCFs. LTCF residents constitute ~10% of the inpatient census at Rush-Presbyterian–St. Luke’s Medical Center (Chicago, Illinois), a 700-bed tertiary care teaching hospital in which VRE is endemic. The purpose of this study was to determine the prevalence of colonization with VRE among LTCF residents admitted to this hospital, to identify risk factors for colonization at the time of admission and for nosocomial acquisition of VRE in this population, and to assess the contribution of LTCF residents to the epidemiology of VRE in an acute care hospital.

METHODS

Study setting and patient population. This was a prospective, observational cohort study of patients in LTCFs who were admitted to two 37-bed general medical wards of Rush-Presbyterian–St. Luke’s Medical Center. The study protocol was approved by the Human...
Investigation Committee, Office of Research Administration, Rush-Presbyterian–St. Luke’s Medical Center.

**Microbiological methods.** Antecubital and rectal swab specimens (S/P Culturette System; Baxter Diagnostics) were obtained from all identified patients in the LTCFs within 72 h after admission to this hospital; for 85% of them, this took place within 48 h after admission [5]. Patients had samples obtained for culture again before discharge or transfer from the ward or at least once more during their hospital stay. Enrollment and sample collection took place during a 33-week period from January through November 1996.

Swab specimens were cultured on bile-esculin agar (Enterococcus; Becton Dickinson Microbiology Systems), which was supplemented with 6 μg/mL of vancomycin, and in bile-esculin broth (Enterococcus; Becton Dickinson Microbiology Systems), which contained 6 μg/mL of vancomycin, as described elsewhere [6]. Putative enterococcal isolates were identified by use of standard methods [7]. Susceptibility to ampicillin and teicoplanin was determined by disk diffusion [8]. Vancomycin resistance was confirmed by use of a microdilution method [9]. Strain types were identified by pulsed-field gel electrophoresis (PFGE) of Smal-digested (Gibco BRL; Sigma) total genomic enterococcal DNA [10]. Strains were considered distinct if their restriction digestion profiles after PFGE differed by >6 bands on visual inspection [11]. vanA, vanB, and vanC1/C2 genotypes were detected by use of PCR assays, as described elsewhere [12].

**Chart review.** We collected demographic and clinical data from patient charts at admission and during the inpatient stay. The patients were examined to identify the presence of pressure ulcers (other than stage 1 ulcers) [13] and to assign a Karnofsky score. Accompanying LTCF transfer records were evaluated for confirmatory information regarding the patient’s functional status, length of stay in the nursing home, and documented antibiotic use in the past 60 days. We also reviewed medical records from earlier hospital stays at Rush-Presbyterian–St. Luke’s Medical Center for evidence of antibiotic use during the 60 days immediately before the index admission and for infections commonly treated with antibiotics, such as sepsis or other infections and urinal tract infection, and considered the latter patients to have had “probable antibiotic use.”

Computer reports of all enterococcal isolates identified in the microbiology laboratory were reviewed to identify clinical isolates of VRE among patients in the study cohort. In addition, we screened the addresses of all patients with clinical isolates of VRE identified during the first 4 months of 1996 to determine the proportion of VRE isolates from LTCF residents.

**Point prevalence surveys.** We determined the point prevalence of VRE rectal colonization in patients on the 2 designated general medical wards by collecting rectal swabs 7 times in an 8-week period that began on 23 January 1996.

**LTCF review.** We reviewed information about the study patients’ LTCFs of origin, which was available from the US Health Care Finance Administration. These data included each LTCF’s census, certified bed capacity, percentage of occupancy, and percentage of patients insured with Medicaid.

**Statistical methods.** Univariate analysis with χ² and Fisher’s exact tests was done for dichotomous variables. Student’s t test was used for continuous variables. Multivariate analysis was done using stepwise logistic regression. Only variables with a P value of ≤.05 on univariate analysis were included in the regression model. The statistical software program used for these analyses was SPSS for Macintosh, version 10 (SPSS). A 2-tailed P value of <.05 was considered statistically significant.

**RESULTS**

**Patients.** One hundred patients were enrolled; 70 patients were women, and 66 were African American. The mean age of study subjects was 78 years (range, 21–106 years), and the mean Karnofsky score was 30 (range, 10–40). Patients were admitted from 20 different LTCFs.

Cultures of samples obtained on admission to the hospital showed that 45 patients were colonized with VRE. These patients came from 15 of 20 LTCFs included in the sample. Forty-two of 55 patients who were not colonized with VRE on admission had additional samples obtained and cultured; 14 (33%) of these patients were subsequently colonized with VRE. Overall, 59% of enrolled patients were found to be colonized with VRE at some time during their index hospitalization.

To determine the risk factors for colonization with VRE on admission, the 45 patients colonized with VRE were compared with the 55 patients without VRE on admission. The following risk factors were identified by univariate analysis: hospitalization in the prior 60 days; an admission diagnosis of infection; inability to ambulate; presence of a feeding tube; urinary catheter, or decubitus ulcer; and documented or probable antibiotic use in the previous 60 days (table 1). Prior antibiotic use was further subdivided into use of vancomycin, cephalosporins, or other antibiotics. Each of these antibiotic groups was a significant risk factor for colonization with VRE.

Stepwise logistic regression analysis identified the presence of a decubitus ulcer on admission to the hospital and documented or probable antibiotic use in the 60 days before admission as significant risk factors for colonization with VRE at the time of admission (table 2).

We sought to identify characteristics of the LTCFs that were associated with an increased rate of colonization with VRE in patients admitted to the hospital. Six LTCFs had >5 patients each enrolled in our study. The LTCF-specific VRE colonization rate among these 6 facilities ranged from 33% to 57%, and there were no apparent quantitative or qualitative differences...
Table 1. Univariate analysis of potential risk factors for colonization with vancomycin-resistant enterococci (VRE) on admission to an acute care hospital.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>LTCF residents</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Colonized on admission (n = 45)</td>
<td>VRE not found (n = 55)</td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>33 (73)</td>
<td>37 (67)</td>
<td>1.3 (0.56–3.1)</td>
</tr>
<tr>
<td>African American race</td>
<td>30 (67)</td>
<td>36 (65)</td>
<td>1.0 (0.45–2.4)</td>
</tr>
<tr>
<td>Age, mean years ± SE</td>
<td>75 ± 2</td>
<td>80 ± 2</td>
<td>NA</td>
</tr>
<tr>
<td>Karnofsky score, mean ± SE</td>
<td>28 ± 1</td>
<td>31 ± 1</td>
<td>NA</td>
</tr>
<tr>
<td>Diagnosis of infection on admission to the hospital</td>
<td>27 (60)</td>
<td>20 (36)</td>
<td>2.6 (1.2–5.9)</td>
</tr>
<tr>
<td>Hospitalization in the 60 days before admission</td>
<td>27 (60)</td>
<td>16 (29)</td>
<td>3.6 (1.6–8.4)</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>4 (8.9)</td>
<td>5 (9.1)</td>
<td>0.97 (0.25–3.9)</td>
</tr>
<tr>
<td>Bedridden</td>
<td>42 (93)</td>
<td>41 (75)</td>
<td>4.8 (1.3–18)</td>
</tr>
<tr>
<td>Use of feeding tube</td>
<td>18 (40)</td>
<td>11 (20)</td>
<td>2.7 (1.1–6.5)</td>
</tr>
<tr>
<td>Use of urinary catheter</td>
<td>26 (58)</td>
<td>17 (31)</td>
<td>3.0 (1.3–7.0)</td>
</tr>
<tr>
<td>Fecal incontinence</td>
<td>39 (87)</td>
<td>44 (80)</td>
<td>1.6 (0.55–4.8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (8.9)</td>
<td>5 (9.1)</td>
<td>0.98 (0.25–3.9)</td>
</tr>
<tr>
<td>Decubitus ulcer</td>
<td>29 (64)</td>
<td>15 (27)</td>
<td>4.8 (2.1–11.3)</td>
</tr>
<tr>
<td>Documented or probable antibiotic use in the 60 days before admission</td>
<td>Any 38 (84)</td>
<td>24 (44)</td>
<td>7.0 (2.7–18.4)</td>
</tr>
<tr>
<td></td>
<td>Vancomycin 9 (20)</td>
<td>0 (0)</td>
<td>13.5 (1.6–111)</td>
</tr>
<tr>
<td></td>
<td>Cephalosporin 10 (22)</td>
<td>3 (5.4)</td>
<td>5.0 (1.3–19)</td>
</tr>
<tr>
<td></td>
<td>Other 26 (58)</td>
<td>15 (27)</td>
<td>3.6 (1.6–8.4)</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of patients, unless otherwise indicated.

in the findings of the LTCF census, bed occupancy rate, or percentage of patients receiving Medicaid that were associated with an increased risk of colonization with VRE.

Nosocomial acquisition of VRE. To determine the risk factors for VRE acquisition in the hospital, we compared the 28 patients who were never colonized with VRE and the 14 patients who acquired VRE in the hospital. Univariate analysis failed to identify any of the 18 tested variables as risk factors for nosocomial acquisition of VRE (data not shown). However, 12 (86%) of 14 patients who acquired VRE colonization in the hospital received antibiotics during their stay, compared with 18 (64%) of 28 patients who did not become colonized with VRE (P = .3). Duration of hospital stay was identical for the 2 groups (mean duration ± SD, 14 ± 2 days).

Skin colonization. Twenty-eight patients were found to have antecubital skin colonization with VRE at some time during their hospitalization; all but 2 of these patients also had rectal colonization.

Strain typing with PFGE and PCR for vancomycin resistance genes. The 45 subjects colonized with VRE on admission to the hospital carried 14 different strain types. We identified 7 vanA Enterococcus faecium strain types, 1 vanA E. faecalis strain type, 1 vanB E. faecalis strain type, and 1 vanA Enterococcus avium strain type. Multiple strain types were isolated from most LTCFs; for example, 9 patients from 1 facility were colonized with 6 different strain types. Strain types also circulated in >1 LTCF; for example, 1 strain type of vanA E. faecium was found in 7 subjects from 5 different LTCFs.

The 14 subjects who became colonized with VRE in the hospital also acquired a variety of strains. Twelve subjects acquired 7 different strains of E. faecium; 1 of these subjects also acquired E. avium. We did not detect nosocomial acquisition of vancomycin-resistant E. faecalis in this previously uncolonized cohort.

Table 2. Stepwise logistic regression analysis for significant risk factors for colonization with vancomycin-resistant enterococci in hospitalized residents of long-term care facilities.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decubitus ulcer present on admission</td>
<td>3.5 (1.4–9.2)</td>
<td>.009</td>
</tr>
<tr>
<td>Documented or probable antibiotic use in the 60 days before admission</td>
<td>4.2 (1.4–12.5)</td>
<td>.008</td>
</tr>
</tbody>
</table>
**LTCF residents’ contribution to the prevalence of VRE on study wards.** The 7 point prevalence surveys for rectal colonization with VRE on the 2 study wards had a collection rate of 83% (i.e., samples were collected on 380 of 457 patient-days when sampling was possible). The mean weekly point prevalence was 30% (113 of 380 cultures were positive), with a range of 11%–50%. Patients in LTCFs constituted 17% of persons who provided samples for culture but 31% of those colonized with VRE. The mean point prevalence among LTCF residents was 60% (49 of 82 cultures were positive), compared with 21% for all others (64 of 298 cultures were positive; P < .001); the prevalence was 29% for the patients who were >60 years of age (mean age, 74 years) who were not LTCF residents (41 of 140 cultures were positive; P < .001). PFGE analysis of VRE isolates from the point prevalence surveys on the study wards showed 14 different strain types. The predominant strain types in these surveys matched the most common strain types among the LTCF study cohort.

**Clinical isolates of VRE.** Only 11 of the 100 enrolled LTCF residents had clinical VRE isolates identified during their index admission or during 11 months of follow-up, including 2 with cases of bacteremia. Throughout the hospital, in the first 4 months of 1996, 68 patients had clinical VRE isolates. Fifteen (22%) of these patients were identified as LTCF residents, although they composed ~10% of the hospital population.

**DISCUSSION**

In this study, we found that hospitalized LTCF residents can carry VRE at very high rates. Almost half of LTCF residents already harbored VRE at the time of admission to the hospital, and many of these residents acquired VRE in the hospital; 59% of the LTCF residents were found to be colonized at some point during their hospital stay. In ward point prevalence surveys, patients from LTCFs were disproportionately (2-fold more frequently) represented among VRE-colonized hospital patients. The frequency of detection of VRE among newly admitted LTCF residents was sustained throughout the study and was not an isolated event for the LTCFs involved.

VRE-colonized patients were admitted from 20 LTCFs, and multiple strain types were detected in patients from each location. These findings suggest that VRE in Chicago have become endemic not just in hospitals, but also in community LTCFs. We did not attempt to determine whether cross-colonization with VRE occurred in the LTCF. However, some of the risk factors for VRE colonization that were identified, such as decubitus ulcers, are likely to be present among LTCF residents who are not hospitalized. Spread of other antibiotic-resistant pathogens among residents of LTCFs is well documented. The presence of a reservoir of VRE-colonized patients among at-risk LTCF residents may provide opportunity for wider dissemination of VRE.

Other recent studies have identified residence in a nursing home as a risk factor for VRE colonization or infection, which suggests that our findings are not unique to Chicago [14]. Bonilla et al. [15] showed that prevalence of VRE colonization among patients in the long-term care unit of the Ann Arbor Department of Veterans Affairs (VA) Medical Center exceeded the prevalence in the intensive care unit and general medical wards. In a separate, freestanding VA LTCF on the East Coast, Brennan et al. [16] found that patients in LTCFs were usually colonized with VRE during an antecedent hospital stay, although person-to-person transmission was also detected. In that study, cultures performed during follow-up showed that fecal VRE carriage was maintained for a median of 67 days before it cleared spontaneously. Person-to-person spread within an LTCF was also suggested when 5 residents in a Canadian facility were colonized with the same strain of VRE—a strain that had not previously been identified in any acute care hospital in the area [17]. A different study failed to show transmission of VRE from 3 known cases to other residents at 3 LTCFs where moderately strict infection-control measures were implemented [18]. In a Centers for Disease Control and Prevention (CDC) investigation of increased VRE incidence in health care facilities in Sioux City, Iowa, patients in LTCFs who had been in an acute care facility were found to be at increased risk for VRE and appeared to act as vectors for regional dissemination to LTCFs. The overall prevalence in the LTCFs evaluated in that study was 1.7% [19].

Our study expands the data on colonization with VRE in LTCF residents. It differs from previous investigations in looking specifically at patients in LTCFs in the hospital, identifying risk factors for colonization in the LTCF population, and including residents from 20 community facilities. This study also included a large number of women, reflecting the LTCF population at large, who were not well represented in the VA facility studies. In our study, the most important risk factors for entering the hospital as a patient already colonized with VRE were the presence of a decubitus ulcer and recent antibiotic use. Recent antibiotic use, recent hospitalization, and poor functional status, such as presence of decubitus ulcers, have been consistent markers of risk for infection or colonization with VRE in the acute care setting [20–26]. Presence of ≥2 of these 3 risk factors would have identified 36 (80%) of our 45 LTCF residents who were colonized with VRE and also put under suspicion an additional 21 patients (38%) without VRE.

This study also expands our knowledge of VRE, by documenting the prevalence of skin colonization in patients with rectal colonization, a phenomenon that we have described elsewhere [6] in patients with bacteremia. Upper-body skin colonization may facilitate person-to-person transmission of VRE.
and transmission through the environment or fomites. Because many hospitals lack the resources to systematically screen patients for VRE carriage, a patient's skin or rectal colonization could go undetected, and contact precautions for the patients might not be instituted. Indeed, only 11 (19%) of 59 VRE-colonized patients in our study cohort would have been identified by the results of clinical cultures alone. Health care workers who touch the intact skin on a patient’s upper body may not perceive themselves to be at risk for contamination with VRE, especially if the patient is not isolated. These findings suggest potential need for a universal gloving strategy in health care settings in which VRE are endemic [27].

Since January 1995, our medical center has followed the Hospital Infection Control Practices Advisory Committee/CDC guidelines for hospitalized patients with VRE. However, the finding of widespread colonization with VRE confounds any attempt at routine isolation of patients according to CDC guidelines [28]. In response to the VRE problem, similarly beleaguered hospitals have adopted various control strategies: stringent controls on antibiotic use, particularly the use of vancomycin and third-generation cephalosporins; cohorting of patients and nursing staff; ward surveillance and environmental surveillance for VRE; and monitored adherence to hand washing and barrier precautions [29–32]. These programs have sometimes been effective in controlling the spread of VRE, but not always. In our analysis of nosocomial colonization with VRE, we found only a single LTCF resident who acquired VRE in the hospital and who had not received antibiotics. Although use of antibiotics was not selected by statistical analysis as a risk factor for nosocomial acquisition of VRE, this may be because antibiotic use was so widespread among the study subjects. Only 47 of our study cohort entered the hospital with a primary diagnosis of infection, yet 82 of the 100 patients received antibiotics. A larger study may be able to discern the specific combinations of antibiotics or the length of antibiotic exposure that may increase risk for nosocomial acquisition of VRE.

There are other limitations to our study. Although we noted that some patients in proximity were infected with the same strain types, the study was not designed to document person-to-person transmission. Also, information regarding previous hospital admissions was limited to those in the previous 60 days. Other studies have shown that colonization with VRE may persist for long periods, and patients may have acquired VRE from less-recent hospital stays [33, 34].

In summary, this study identifies a large number of LTCF residents who entered the hospital with asymptomatic VRE carriage. LTCF residents who are hospitalized probably represent a subset of patients who are ill enough to have enough hospital stays to allow them to encounter VRE and who have substantial antibiotic exposures that provide selective pressure. Indeed, 33% of the subjects in our cohort were newly colonized with VRE during 1 hospital stay. Colonized LTCF residents may migrate between the LTCF, community hospitals, and referral medical centers, and they may act as a reservoir for the transmission of VRE to other patients in these facilities. Clinicians should recognize that LTCF residents who are hospitalized, especially those who have decubitus ulcers or who recently have received antibiotics, are at high risk for VRE carriage. When caring for these patients, appropriate infection control precautions should be taken to limit cross-transmission of VRE.

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References


