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Short Communication

Healthcare-Associated Risk Factors of Vancomycin-Resistant Enterococci Colonization among Outpatients Undergoing Hemodialysis

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SUMMARY: Stool specimens and data were obtained from 399 outpatients undergoing hemodialysis (HD) in order to estimate the colonization rate of vancomycin-resistant enterococci (VRE) and to determine risk factors for VRE acquisition. The prevalence of VRE colonization in outpatients ranged from 0%–22.2%. Risk factors associated with VRE colonization were high hierarchy of hospital, short duration of HD, recent hospitalization, prior use of antimicrobial products, high platelet count, and low hemoglobin/albumin/blood urea nitrogen/creatinine levels, showing that VRE colonization was more common in patients with prior infections and poor nutritional status. Although pulsed-field gel electrophoresis (PFGE) analysis showed that most VRE isolates had diverse patterns, 2 paired cases from separate hospitals presented identical PFGE types.

Vancomycin-resistant enterococci (VRE) are a growing source of nosocomial infections worldwide. Patients undergoing hemodialysis (HD) for chronic renal failure are at high risk of VRE acquisition due to several factors such as the close contact between patients in the dialysis unit, presence of comorbid conditions, repeated exposure of patients to antibiotics, and frequent hospitalization. Outpatient HD patients are frequently exposed to healthcare-associated risk factors similar to that of nosocomial diseases. We conducted a cross-sectional multicenter survey to investigate colonization rates, risk factors, and molecular relatedness of VRE among outpatients in HD units in Korea, which included primary clinics, and secondary and tertiary hospitals.

Stool specimens were obtained from 399 outpatients who underwent HD between August 2005 and September 2005. The outpatients underwent maintenance HD at 12 dialysis units located in a southwestern area of Seoul, Korea. Patients from 7 primary clinics, 1 secondary hospital, and 4 tertiary hospitals were included in the study. Data including demographics, findings of laboratory tests, comorbidities, and history of antimicrobial use and hospital admission in 6 months before study inclusion were collected from the outpatients. All stool cultures were processed by the standard methods for VRE identification, as described previously (1). Polymerase chain reaction (PCR) was performed to determine the glycopeptide resistance genotypes and confirm the species; PCR was performed, as previously described (1) using the oligonucleotide primers described by Song et al. (1) and Dukta-Malen et al. (2). The molecular relatedness of the pulsed-field gel electrophoresis (PFGE) patterns of VRE isolates was assessed according to the criteria described by Tenover et al. (3), and additional detailed comparisons were performed using computer-assisted analysis (GelCompar version 4.1; Applied Maths, Kortrijk, Belgium). The unweighted pair-group method using arithmetic averages (UPGMA) was applied, and the bandwidth tolerance was critically set at 4.0%. Data processing and evaluation were performed using the SPSS 19.0 (SPSS Inc. Chicago, Ill., USA).

Of the 399 patients, 18 patients (4.5%) carried VRE in their gastrointestinal tract. The prevalence of VRE colonization was remarkably different according to the hierarchy of hospitals (Table 1). Colonization rates in primary clinics or secondary hospitals were less than 2%, whereas the rates in tertiary hospitals ranged from 5.3%–22.2% with an average of 13.3%. Of the 18 VRE isolates, 13 strains were identified as *Enterococcus faecium*, and the remaining 5 strains were identified as *E. faecalis* (2 strains), *E. gallinarum* (2 strains), and *E. casseliflavus* (1 strain). The 13 *E. faecium* and 2 *E. faecalis* strains were highly resistant to vancomycin (minimum inhibitory concentration [MIC], >256 mg/L) and teicoplanin (MIC, 16–>256 mg/L); these strains were of the *vanA* phenotype. The remaining 2 *E. gallinarum* and 1 *E. casseliflavus* strains were of the VanC phenotype and showed low resistance to vancomycin (MIC, 6 mg/L) and susceptibility to teicoplanin (MIC, 0.5–0.75 mg/L).

Analysis of PFGE banding patterns of 13 *E. faecium* and 2 *E. faecalis* isolates was perfomed according to the

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**Members of the Western Dialysis Physical Association are listed in the appendix.

Table 1. Comparison of vancomycin-resistant enterococci (VRE) colonization rates according to the hierarchy of hospitals

Primary clinic and secondary hospital				Tertiary hospital			
Clinic or hospital	No. of patients	VRE (%)	VRE species	Hospital	No. of patients	VRE (%)	VRE species
A clinic	52	0		I hospital	41	8 (19.5)	7 *E. faecium*, 1 *E. faecalis*
B clinic	48	0		J hospital	36	3 (8.3)	3 *E. faecium*
C clinic	49	1 (2)	1 *E. faecium*	K hospital	9	2 (22.2)	2 *E. faecium*
D clinic	11	0		L hospital	19	1 (5.3)	1 *E. casseliflavus*
E clinic	46	1 (2.2)	1 *E. gallinarum*				
F clinic	38	2 (5.3)	1 *E. faecalis*, 1 *E. gallinarum*				
G clinic	15	0					
H hospital	35	0					
Subtotal	294	4 (1.4)		Subtotal	105	14 (13.3)	

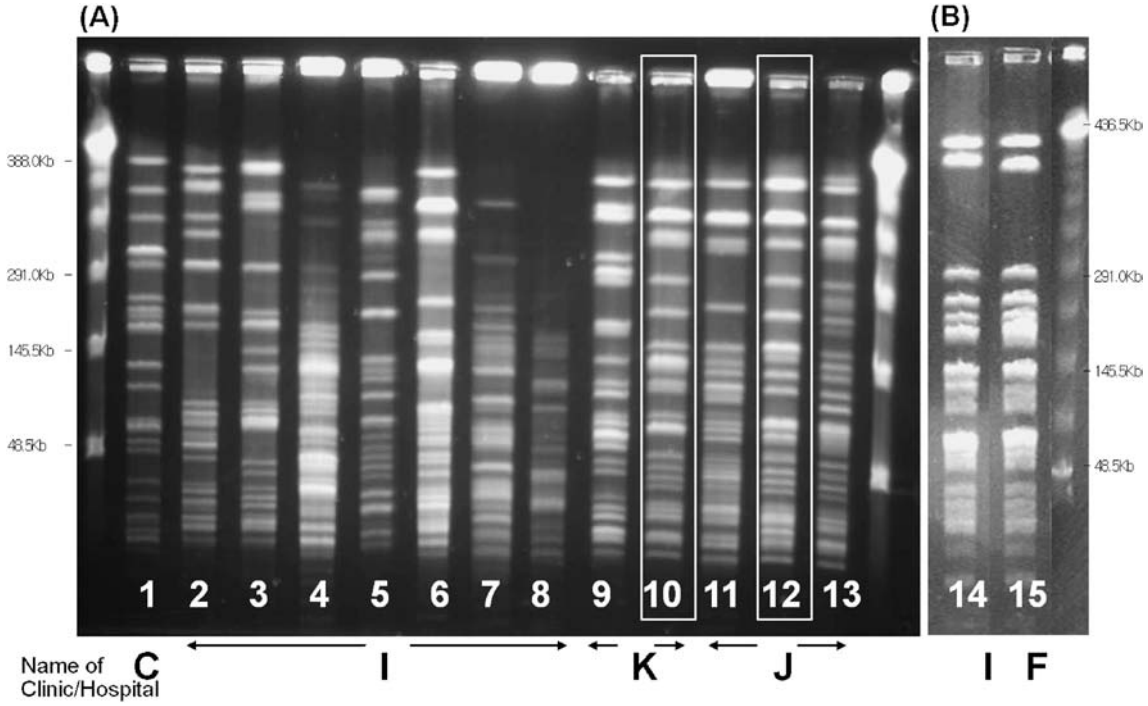

Fig. 1. (A) PFGE types of vancomycin-resistant *Enterococcus faecium* isolates. Most of them showed diverse banding patterns, but strains with similar subtypes were recovered from separate facilities (strain nos. 10 and 12). (B) PFGE types of vancomycin-resistant *Enterococcus faecalis* isolates. The two strains from two different medical facilities show same banding patterns.

criteria described by Tenover et al. (3), and the results are shown in Fig. 1. Most of the isolates displayed diverse patterns with no similarity, and no genetically identical strains were identified from the same hospital. However, 2 *E. faecium* strains (strain nos. 10 and 12) from 2 distantly located tertiary hospitals had a similar band pattern and 2 *E. faecalis* strains (strain nos. 14 and 15), one from a tertiary hospital and the other from a neighboring primary clinic, also showed nearly identical PFGE patterns. Dendrogram analysis of 13 *E. faecium* strains revealed that strain nos. 10 and 12 were genetically identical, while the other strains showed less than 75% similarity (Fig. 2).

Risk factors that showed statistically significant association with VRE colonization were as follows: high hierarchy of hospital, short duration of HD, hospitalization within 6 months, prior use of antimicrobials such as cephalosporins, quinolones, and vancomycin within 6 months, high platelet count, and low hemoglobin, blood urea nitrogen (BUN), creatinine, and albumin levels (Table 2).

In the present study, the overall colonization rate was estimated as 4.5%, this value is not higher than that reported from western countries (4), but some tertiary hospitals had high colonization rates up to approximately 20%. Compared to patients with no VRE colonization, VRE-colonized patients had undergone HD for shorter duration; this may be because patients with short HD duration were more likely to have been recently exposed to antibiotics and hospitalized at the initiation of HD. In fact, the duration of HD for patients who had recently used antibiotics was shorter than that

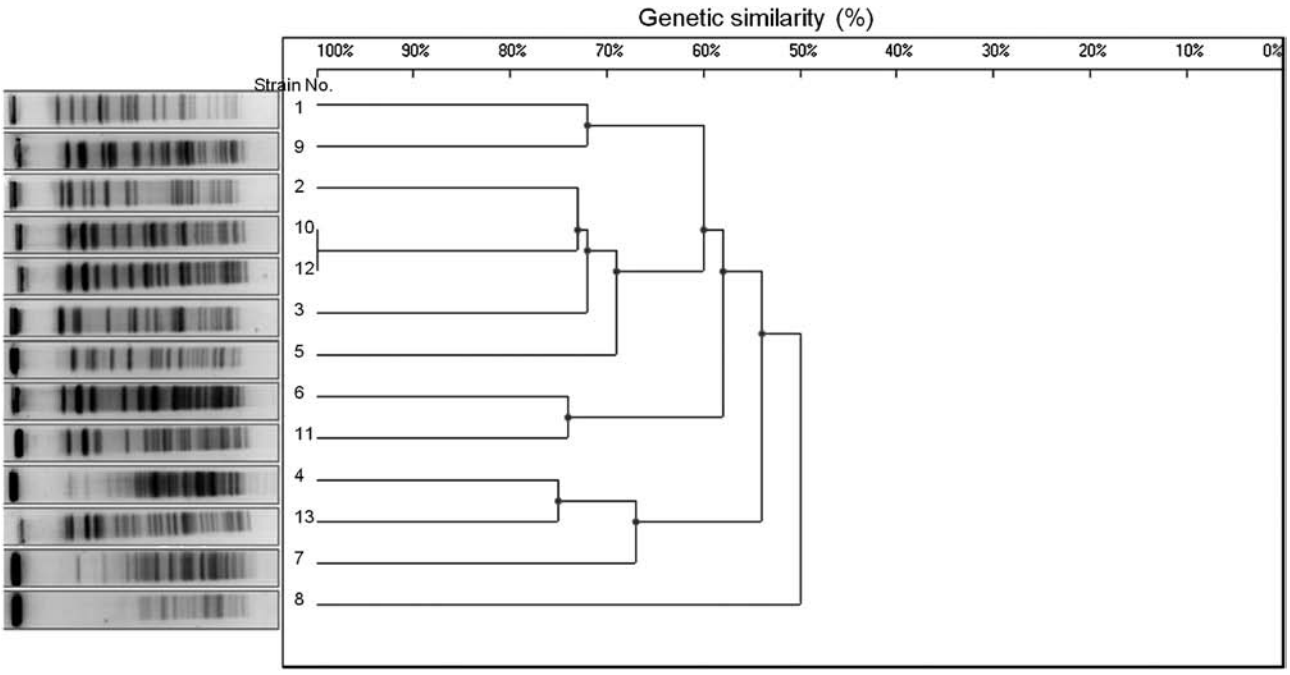

Fig. 2. Dendrogram of vancomycin-resistant *Enterococcus faecium* isolates from outpatients undergoing dialysis. One paired strains (strain nos. 10 and 12) were similar to each other and others were different with the tolerance at 5.0%.

Table 2. Risk factors for VRE acquisition

	VRE positive	VRE negative	P[1]
Mean age (mean ± SD)	58.71 ± 9.60	55.02 ± 12.69	0.240
Male gender	8 (44.4%)	165 (50.8%)	0.601
High hierarchy[2]	13 (72.2)	125 (32.8)	<0.001
HD duration (mo)	17.83 ± 21.13	51.31 ± 51.38	<0.001
Body weight (kg)	55.34 ± 9.92	56.59 ± 9.61	0.613
Systolic BP (mmHg)	135.63 ± 11.16	143.29 ± 17.88	0.230
Diastolic BP (mmHg)	79.38 ± 12.66	82.98 ± 10.00	0.450
Diabetes	9 (64.3%)	107 (41.8%)	0.098
Hypertension	6 (42.9%)	89 (34.8%)	0.537
Hospital admission[3] (%)	13 (72.2%)	59 (20.4%)	<0.001
Antimicrobial use[3]	14 (77.8%)	103 (35.4%)	<0.001
Cephalosporin	13 (72.2%)	78 (26.8%)	<0.001
Quinolone	8 (44.4%)	22 (7.6%)	<0.001
Vancomycin	4 (22.2%)	11 (3.8%)	0.007[4]
Leukocyte (10^3/mm^3)	7.58 ± 3.39	6.29 ± 2.01	0.126
Hemoglobin (g/dL)	9.51 ± 1.35	10.40 ± 1.17	0.002
Platelet (10^3/mm^3)	222.06 ± 97.37	184.43 ± 67.99	0.028
BUN (mg/dL)	47.46 ± 16.50	63.76 ± 19.80	0.001
Creatinine (mg/dL)	6.90 ± 2.78	9.86 ± 2.85	<0.001
Serum albumin (g/dL)	3.31 ± 0.63	3.94 ± 0.40	0.001

[1]: χ^2 test.
[2]: Tertiary hospitals.
[3]: During the past 6 months.
[4]: Fischer's exact test.
HD, hemodialysis; BP, blood pressure, BUN, blood urea nitrogen.

for patients who had not used antibiotics recently (47.7 months versus 53.9 months). In addition, since our study population was limited to outpatients, patients who underwent HD for long duration were more likely to be in better health and, therefore, less likely to be colonized by VRE than patients who underwent HD for short duration. VRE colonization was related to poor nutritional and hypermetabolic state, which is indicated by the low levels of blood hemoglobin, serum albumin, and BUN in VRE-colonized patients. Previous studies reported an epidemiologic relation with similar PFGE patterns in hospitalized HD patients (5), but there was no evidence of intrahospital spread in this study. However, VRE strains with similar subtypes were isolated from separate facilities. The 2 facilities with similar PFGE types were located near each other and many patients visit both the facilities. Although the patients with similar VRE strains in the present study had no history of contacting each other or visiting the other facility, hospitals in nearby regions may be readily contaminated with VRE from other patients and thus, inter-facility transmission may have occurred. A previous study reported that 29% of the environmental contamination occurred after single outpatient visits by 7 VRE-colonized patients (6). In another study, 36%–58% of chairs and couches were contaminated with VRE after being exposed to VRE-colonized patients (7).

Though VRE colonization was not problematic in the HD units of private clinics, the colonization rates were markedly high in tertiary hospitals. VRE colonization was more common among patients with prior infections and poor nutritional status. No evidence of intrahospital spread of VRE strains was noted, but the possibility of inter-facility transmission was detected. Further studies are needed to investigate such a possibility, and strict infection control strategies and careful management should be adopted in outpatient settings to reduce further infections.

Conflict of interest None to declare.

Appendix The following are the members of Western Dialysis

Phyisican Association: Hwa Jeong Kim (Yein Medical Clinic, Seoul, Korea), Young A. Kim (Yonsei Medical Clinic, Seoul, Korea), Jong Young Lee (Onuri Hemodialysis Center, Seoul, Korea), Hun Kwan Lim (Woori Internal Medicine, Seoul, Korea), Rho Won Chun and Sung Tae Cho (Dr. Chun & Cho's Medical Clinic & Dialysis Center, Seoul, Korea), Kyung Shik Oh (Dr. Oh's Hemodialysis Center, Seoul, Korea), Seong Nam Kim (Dr. Kim's Medical Clinic, Seoul, Korea), Kyung Wook Kim (Gwangmyung Sung Ae General Hospital, Kyungido, Korea), Suk Hee Yu and Dong Jin Oh (Department of Internal Medicine, Chung Ang University, Seoul, Korea), Kyu Bok Choi and Seung Jung Kim (Division of Nephrology, Department of Internal Medicine, Ewha Woman's University Mokdong Hospital, Seoul, Korea).

REFERENCES

1. Song, J.Y., Hwang, I.S., Eom, J.S., et al. (2005): Prevalence and molecular epidemiology of vancomycin-resistant enterococci strains isolated from animals and humans in Korea. Korean J. Intern. Med., 20, 55–62.
2. Dutka-Malen, S., Evers, S. and Courvalin, P. (1995): Detection of glycopeptide resistance genotypes and identification to the species level of clinically relevant enterococci by PCR. J. Clin. Microbiol., 33, 24–27.
3. Tenover, F.C., Arbeit, R.D., Goering, R.V., et al. (1995): Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J. Clin. Microbiol., 33, 2233–2239.
4. Roghmann, M.C., Fink, J.C., Polish, L., et al. (1998): Colonization with vancomycin-resistant enterococci in chronic hemodialysis patients. Am. J. Kidney Dis., 32, 254–257.
5. D'Agata, E.M., Green, W.K., Schulman, G., et al. (2001): Vancomycin-resistant enterococci among chronic hemodialysis patients: a prospective study of acquisition. Clin. Infect. Dis., 32, 23–29.
6. Smith, T.L., Iwen, P.C., Olson, S.B., et al. (1998): Environmental contamination with vancomycin-resistant enterococci in an outpatient setting. Infect. Control Hosp. Epidemiol., 19, 515–518.
7. Grabsch, E.A., Burrell, L.J., Padiglione, A., et al. (2006): Risk of environmental and healthcare worker contamination with vancomycin-resistant enterococci during outpatient procedures and hemodialysis. Infect. Control Hosp. Epidemiol., 27, 287–293.