

## Hospital-Acquired Vancomycin-Resistant *Enterococci*: A Report of 2-year Experience

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**Abstract-** Vancomycin-resistant *enterococci* (VRE) are becoming a major concern in medical practice. Their increased prevalence and their ability to transfer vancomycin resistance to other bacteria have made them a subject of close scrutiny and intense investigation. Colonization is usually acquired by susceptible hosts in an environment with a high rate of patient colonization with VRE. The aim of this study was to define the prevalence and risk factors of infections with VRE in Amir-Alam Hospital (Tehran, Iran). Fecal samples of 422 newly admitted patients (Group A) and 93 patients with either at least 48-hours of hospitalization or chronic renal failure under hemodialysis (group B) were evaluated for VRE isolates by MIC method in microbiology laboratory in Pasteur Institute of Iran. Stool cultures were positive for *enterococci* in 310 (73.4 %) and 89 (95.7 %) patients in group A and B, respectively. The prevalence of VRE isolates was 1.42 % (6 patients from 422) in group A and 7.52 % (7 patients from 93) in group B by MIC method ( $P < 0.05$ ). In group A, a significant relationship was found between the VRE colonization and underlying conditions like as history of hospitalization and surgery within previous year and antibiotic therapy within three months ago. Prevalence of VRE colonization is increasing in hospitals. Our results indicate the importance of underlying diseases as risk factors for VRE colonization.

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**Key words:** Vancomycin; *enterococci*, gastrointestinal, risk factors

### Introduction

*Enterococci* are part of the normal gut flora of almost all humans. They are capable of causing infections both in and out of the hospital setting. However most enterococcal infections occur in hospitalized patients. Currently, *enterococci* rank second or third in frequency as causes of nosocomial infections in United States.

During 1989-1997, the National Nosocomial Infections Surveillance System reported that the percentage of vancomycin-resistant *enterococci* in nosocomial infections increased from 0.4% to 23.2% among patients in intensive care units and from 0.3% to 15.4% among patients in noncritical care units (1). Since 1997, rates of vancomycin-resistant *enterococci* have continued to increase in both clinical settings (2). Previous hospital-based studies have shown that infection or colonization with vancomycin-resistant *Enterococcus faecium* is associated with prolonged hospitalization, patient transfer between floors, use of vancomycin and third-generation

cephalosporins, and duration of vancomycin use (3, 4, 5). Despite the institution of infection-control measures, including restriction of vancomycin use, vancomycin-resistant *Enterococcus faecium* remains endemic in many hospitals, especially in large tertiary care centers (2, 3). Bacterial infections caused by drug-resistant organisms have historically been associated with increased duration of hospitalization and higher mortality rates, compared with bacterial infections caused by drug-susceptible organisms, regardless of the pathogen (5, 6). We conducted a prospective cross-sectional study to determine the prevalence and risk factors of stool colonization with vancomycin-resistant *enterococci* (VRE) in Amir-Alam Hospital (a tertiary referral center in Tehran, Iran).

### Patients and Methods

This cross-sectional study was performed from January 2006 to December 2007 in Amir-Alam Hospital. A total

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of 422 consecutive adult patients immediately after admission (group A) and a total of 93 patients including 78 patients with either at least 48-hours of hospitalization (range: 2 days to 3 weeks; mean: 5.6 days) and 15 patients with chronic renal failure under hemodialysis 3 times a week (group B) enrolled in the study. A written consent was obtained from each patient. The past medical history of the patients including the history of hospital and ICU admission and surgery within the past recent year and the history of the antibiotic therapy within the past three months was obtained by the physician. Fecal samples of patients were provided by either stool examination in group A or rectal swab in group B. All of the samples were submitted to microbiology laboratory of Pasteur Institute of Iran.

Faecal samples were diluted with sterile saline and plated onto enterococcosel agar (BBL Microbiology Systems, Cockeysville, MD, USA) with and without 6 mg/L of vancomycin. Plates were incubated at 37°C and read after 24 h of incubation. From each sample, colonies showing macroscopically morphological differences and whose colony morphology was consistent with that of *enterococci* were subcultured and characterized as *enterococci* by additional tests (salt tolerance, growth on bile-aesculin azide agar, catalase activity). Identification to species level was carried out with the automated Vitek system (BioMérieux, Marcy l'Étoile, France).

For all distinct enterococcal isolates that grew on the screening agar supplemented with 6 mg/L of vancomycin, MIC of vancomycin was determined by an agar dilution method (7). Interpretative criteria for susceptibility status were those of the National Committee for Clinical Laboratory Standards (7). The results of the study were analyzed by applying Chi square test and  $P < 0.05$  was considered as statistically significant.

## Results

We collected 310 (73.4%) enterococcal isolates from stool samples of Group A and 89 (95.6%) enterococcal

isolates from rectal swab samples of Group B. Thirteen VRE strains were isolated: 6 (1.42%) from Group A patients and 7 (7.52%) from the patients of Group B ( $P < 0.05$ ).

As shown in Table 1, VRE positive patients in Group A had a significantly higher prevalence of history of hospitalization within previous year, antibiotic exposure within three months ago, and history of surgery during last year compared with VRE negative patients ( $P < 0.05$ ). There were no statistically significant differences between VRE positive and negative patients regarding the above mentioned risk factors in Group B (Table 1).

## Discussion

The first isolates of high-level VRE were reported from the United Kingdom in the late 1980s (8). Since then, rates of VRE colonization and infection have risen steadily (9). In the United States, hemodialysis patients have a 10% prevalence rate of colonization with VRE (10). A recent multicenter epidemiological study showed that 28% of *enterococci* cultured from 25 North American intensive care units (ICUs) were resistant to vancomycin (11). Clearly, clinicians need to be aware of the importance of VRE. The aim of this study was to determine the prevalence and risk factors of stool colonization with VRE in a tertiary referral center in Tehran, Iran.

Infection with VRE (described in more detail subsequently) typically follows vancomycin-resistant enterococcal colonization, predominantly of the gastrointestinal tract. Colonization, which does not result in symptoms, may last for long periods and may serve as a reservoir for the transmission of VRE to other patients. As our results showed; within hospitals, widespread colonization with VRE may occur (1.42 % vs. 7.52 % in group A and B, respectively).

**Table 1.** Prevalence of studied risk factors between the two groups

	Group A (n = 422)		Group B (n = 93)	
	VRE (+) (n = 6)	VRE (-) (n = 418)	VRE (+) (n = 7)	VRE (-) (n = 86)
Hx. of hospitalization within previous year	4 (66.7%)*	146 (35%)	2 (28.6%)	27 (31%)
Antibiotic exposure within last 3 months	4 (66.7%)*	58 (14%)	1 (14.3%)	32 (37.2%)
Hx. of surgery during last year	3 (50%)*	121 (29%)	2 (28.6%)	20 (23.2%)
Hx. of ICU admission	0 (0%)	18 (4.3%)	0 (0%)	2 (2.3%)

\* $P < 0.05$

Therefore, increasing the length of hospitalization is a major factor for VRE acquisition and tracking colonization with VRE through active surveillance in high-risk units could be an important component of preventing further transmission.

Colonization is contingent on exposure to VRE and on being a "susceptible" host. With regard to exposure to VRE, the most important considerations are proximity to and duration of exposure to those already colonized with VRE. When the proportion of patients colonized with VRE on a particular ward (the so-called colonization pressure) is high (>50%), other risk factors for colonization (described subsequently) become less important (12). "Susceptible hosts" are at high risk for VRE colonization (12). These include patients who are severely ill and those receiving multiple and prolonged courses of antimicrobial agents. The above issue was also confirmed by our results which showed the significant higher prevalence of studied risk factors in VRE positive patients in group A. There was no significant difference between history of ICU admission and VRE colonization in group A. The reason of this could be due to reduced length of ICU admission. Colonization in susceptible hosts often occurs in long-term care facilities and urban referral hospitals (such as our hospital). Most patients colonized with VRE will remain colonized for prolonged periods. A Mayo Clinic study that defined clearance as negative rectal VRE cultures on at least 3 consecutive tests obtained more than 1 week apart showed spontaneous decolonization in only 18 (34%) of 53 liver and kidney transplant recipients (13). Furthermore, VRE were detected on subsequent surveillance cultures from 2 of these previously decolonized patients (13).

A recent University of Maryland mathematical model showed that active surveillance in the ICU reduced VRE transmission by a projected 39% (14). Another recent study showed annual savings of more than \$400,000 as a result of gown use in a facility with a high prevalence rate of VRE (15). Thus, we recommend active surveillance for hospital populations at high risk (as previously described) for colonization with VRE. Infection with VRE usually develops in patients colonized with the bacteria (16), with the ratio of infected-to-colonized patients dependent on the specific patient population. It is highest in hematology patients and organ transplant recipients and approaches zero in healthier (immunocompetent) populations (16-19). Risk factors for VRE bacteremia include hemodialysis; organ transplantation; receipt of corticosteroids, chemotherapy, or parenteral nutrition; surgery; severe illness; long-

term antibiotic administration; indwelling urinary catheters; neutropenia; and mucositis (20). In conclusion, the prevalence of VRE colonization is increasing in hospitals. The shortening of hospitalization, avoidance of unnecessary admissions and surgical procedures and making a guideline for logical usage of antibiotics could be effective in reducing rate of VRE colonization. For active surveillance of VRE and prevention of major outbreaks, we suggest other studies with large population.

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