Clinical, Epidemiological, and Microbiological Profile of Patients with Vancomycin-Resistant *Enterococci* from a Tertiary Care Hospital

Sir,

Progress in medical technology and the intensive use of broad spectrum antibiotics have been responsible for the emergence of *Enterococci* as important nosocomial pathogens. Although the frequency of isolation of Vancomycin-Resistant *Enterococci* (VRE) is currently not very high in India,[1] this may just be the beginning of the problem, in contrast to the USA and Europe, where VRE appeared in the late 1980s.

Treatment options and effective antimicrobial agents for VRE are often limited and the possibility of the transfer of vancomycin-resistant genes to other Gram-positive microorganisms remains.

We attempted to analyze the clinical, microbiological, and epidemiological features of patients who were culture positive for VRE in a tertiary care hospital in Southern India.

The study was performed at a 600-bed tertiary care hospital, which also conducted kidney and liver transplants. The medical records of 18 patients with a positive culture for VRE were reviewed. A microbiological data analysis was done, which included minimum inhibitory concentration (MIC) to various drugs. The MIC was estimated using the E test. MICs were interpreted based on the latest Clinical and Laboratory Standards Institute (CLSI) guidelines.[2]

In North America and Europe, VRE now accounts for about 30% of the Enterococcal infections, with most VRE isolates being *E. faecium* (>90%).[3] In our study VRE was isolated in 18 [4%] out of 450 isolates of *Enterococci*, all isolates being *E. faecium,* similar to a study from North India which also had the same species of *Enterococci,* with a 10% VRE prevalence. Other studies from North India have shown that only 2–3% of enterococcal isolates were resistant to vancomycin. The VRE prevalence rate was about 3% in our sister cancer hospital,[1] which was similar to our findings.

The most common comorbidities in our study were renal failure and diabetes. One-third of our patients with renal failure were on hemodialysis. Similar to other studies,

prolonged hospitalization was a risk factor for VRE acquisition, as the average length of stay of our patients was 23 days, and average time before VRE isolation was 12 days.

Antibiotic selective pressure, exerted by the extensive use of third generation cephalosporins and drugs with potent activity against anaerobes have been reported to predispose to VRE colonization and infection. A recent case-control study found that the use of parenteral metronidazole as well as of third-generation cephalosporins was highly significant, and were independent risk factors for the isolation of VRE. We found that prior cephalosporin and vancomycin exposure was present in 94% and 55%, respectively.

In our study urine was the most common specimen from which VRE was isolated. Studies on the epidemiology of nosocomial urinary tract infection (UTI) caused by vancomycin susceptible *Enterococci* have shown urinary catheterization to be an important predisposing factor, present in 82 to 95% of the patients. A urinary catheter was present in 13 of our patients.

Five patients had VRE bacteremia. In our study, 11 patients had a central line. Recent data suggest that *E. faecium* bloodstream infection may have a worse prognosis than *E. faecalis*, probably because these organisms are much more resistant to antibiotics and are increasingly difficult to treat. In one study, an independent risk factor for death was VRE bloodstream infection (BSI). In our study four out of the five patients with bacteremia survived.

Recent surveillance from US hospitals showed more than 99.5% VRE isolates susceptible to daptomycin. Studies show no significant mortality difference between patients treated with linezolid and daptomycin.[4] One study from a tertiary care hospital in south India[3] showed that daptomycin was active against all *Enterococcus* spp., including VRE. The daptomycin MIC values for the VRE isolates ranged from 1 mg / mL to 4 mg / mL (100% susceptibility), with 90% of the *E. faecium* strains inhibited at 2 mg / mL daptomycin. A study from north Indian hospitals, where daptomycin was the single-most active compound, showed all strains inhibited by 4 μg / ml.[5] However, daptomycin resistance in *Enterococci* may be emerging. A very recent study has also shown the emergence of resistance to daptomycin by a previously sensitive *E. faecalis* isolate, while on therapy.[6] In our study 14 out of 18 (77%) isolates had high daptomycin MICs. Without susceptibility data, daptomycin should therefore be used with caution for empiric therapy, for serious VRE infections.

Linezolid seemed to be an appropriate therapeutic option for VRE in our study, as 12 of our isolates had a MIC of 2 or less.

Tigecycline sensitivity was performed on four of our isolates and they were found to be sensitive. Isolates from a study in North India showed 100% sensitivity to tigecycline,[7] similar to a study from South Korea. More studies on tigecycline for serious VRE infections are needed.

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