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ORIGINAL RESEARCH

Distribution Of Vancomycin Resistant Enterococci (VRE) Among Various Clinical Isolates And Vancomycin Resistant Phenotypes Suggested By Vitek 2C Automated System

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Abstract:
Introduction: Antimicrobial resistance is among the top 10 global health threats. We analyzed the distribution pattern of VRE among various clinical isolates and Vancomycin resistant phenotypes suggested by Vitek 2C automated system in this study.
Material & Methods: A retrospective analysis of VRE isolates from various clinical specimens obtained from Jan 2022 to Dec 2022 at a tertiary care center was done. The isolates were identified to species level using Vitek 2C system using GP ID & P628 cards.
Results: During this period, a total of 32 VRE isolates were identified out of which 43.75% were from males and 56.25% were from females. Amongst the VRE isolates (n=32), most common was *E.faecium* (50%) followed by *E.gallinarum* (9.37%), *E.faecalis* (6.25%), *E.avium* spp (6.25%) *E. casseliflavus* (3.12%). The distribution in clinical specimen was pus specimens (43.75%), urine (40.62 %), blood (9.37%), ascitic fluid (6.25%). Out of 32 VRE isolates, Vancomycin resistant phenotypes were suggested by Vitek 2C in 28 isolates. Most common was Van A phenotype, in 14 isolates of *E. faecium*, 02 isolates of *E.faecalis*, 01 isolate of *E. casseliflavus*, 01 in *E. gallinarum* , whereas Van B in 02 isolates of *E.faecium.* 08 VRE isolates could not be identified upto species level, had Van A type in 7 isolates and Van B type in 01 isolate.
Conclusion: Among the observed VRE isolates, our study found a higher frequency of *E. faecium* than *E. faecalis* and majority of VRE were of Van A phenotype. In resource limited settings, automated identification systems can give a clue towards possible phenotypes so that necessary infection control practices can be implemented.
Keywords: VRE, resistance, phenotype, automated system.

Introduction:

Antimicrobial resistance is among the top 10 global health threats. [1] *Enterococci* has been recognized as organisms of global concern and prioritized as high-priority pathogens due to emergence of vancomycin resistance (Vancomycin resistant enterococci, VRE) in clinical specimens.[2]. We analysed the distribution pattern of VRE among various clinical isolates and Vancomycin resistant phenotypes suggested by Vitek 2C automated system in this study.

Material & Methods:

A retrospective analysis of VRE isolated from various clinical specimens obtained from Jan 2022 to Dec 2022 at a tertiary care center was done. The isolates were identified to species level using Vitek 2C automated system using GP ID & antimicrobial susceptibility was done using AST P628 cards. Vancomycin phenotypes suggested by Vitek 2 system, were also analyzed.

Results:

During this period, 32 VRE isolates were identified, out of which 43.75% were from males and 56.25% were from females. The distribution of VRE in clinical specimen was pus specimens (43.75% n=14/32), urine (40.62 %, n=13/32), blood (9.37%, n=3/32) & ascitic fluid (6.25%, n=2/32) **(Table 1)**. Amongst the VRE isolates (n=32), most common was *E. faecium* (50%, n=16/32) followed by *E. gallinarum* (9.37%), *E.*

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faecalis (6.25%, n=02/32), *E. avium* (6.25%, n=02/32) & *E. casseliflavus* (3.12%, n=01/32) (**Table 1).**

Table 1: Distribution pattern of VRE in various clinical specimens.

	E. faecium	E. faecalis	E.gallinarum	E.casseliflavus	E.avium	Enterococcus spp
PUS	8	0	2	0	2	2
ASCITIC FLUID	2	0	0	0	0	0
BLOOD	0	0	0	0	0	3
URINE	6	2	1	1	0	3

Out of 32 VRE isolates, Vancomycin resistant phenotypes were suggested by Vitek 2C in 28 isolates. Most common was Van A phenotype, in 14 isolates of *E. faecium*, 02 isolates of *E.faecalis*, 01 isolate of *E. casseliflavus*, 01 in *E. gallinarum* ,whereas Van B in 02 isolates of *E.faecium*. 08 VRE isolates could not be identified upto species level, Van A type was suggested in 7 such isolates and Van B type in 01 isolate. **(Table 2)**

Table 2: Distribution of Vancomycin resistant phenotypes as suggested by Vitek 2C automated system.

Total	Van A	Van B
E. faecium	14	02
E.faecalis	02	-
E.casseliflavus	01	-
E.gallinarum	01	-
Enterococcus spp.	07	01

In pus samples, *E. faecium* was most common (25 %, n=8/32) followed by *E. gallinarum* (6.25%, n=2/32) & *E .avium* (6.25%, n=02/32), whereas species could not be identified in 02 Enterococcus isolates. Both the isolates from ascitic fluid were identified as *E. faecium* (6.25%, n=02/32). 03 isolates identified from Blood could not be identified upto spp. level. In Urine, 06 isolates were identified as *E. faecium* (15.375 %, n=6/32), 02 as *E. faecalis* (6.25%, n=02/32), 01 as *E. gallinarum* (3.125%, n=1/32), 01 as *E. casseliflavus* (3.125%, n=1/32). (**Table 3)**

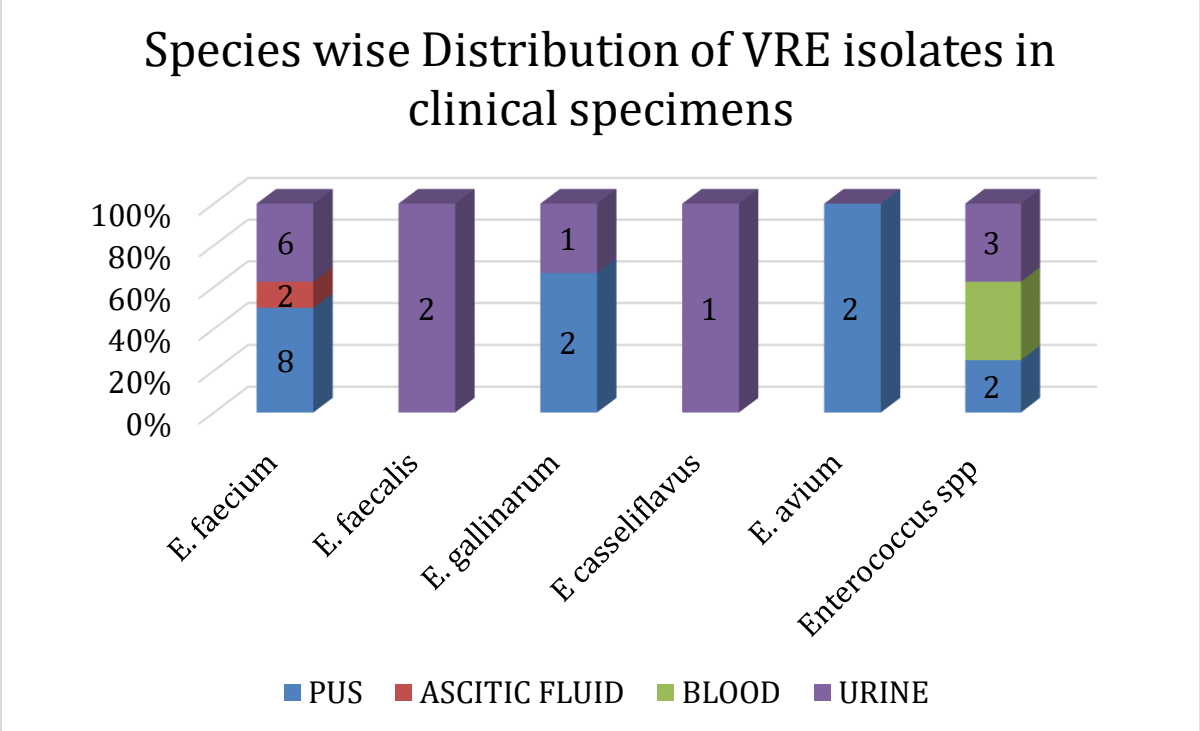

Table 3: Species wise distribution of VRE isolates in clinical specimens.

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Discussion:

Enterococci are known commensals of the human gastrointestinal tract, with lesser frequency in the vagina and mouth and can cause various human infections like urinary tract infections, bacteraemia, endocarditis, and surgical site infections and importantly nosocomial infections. [3] They can acquire resistance to vancomycin, a glycopeptide antibiotic which inhibits bacterial cell wall synthesis, whereas intrinsic, low-level vancomycin resistance has been reported in *E. gallinarum* and *E. casseliflavus* with MICs ranging to 32 µg/ml.[4, 5]

Although recognized globally now, VRE isolates were initially reported in France by Leclercq et al in 1986 [6] and then in 1988, by Uttley et al in England. [7]

In our study maximum VRE isolates were isolated from pus specimens (43.75%), followed by urine (40.62 %), blood (9.37%) & ascitic fluid (6.25%) in decreasing order. Ira et al also reported maximum cases from pus and wound swabs followed by urine.[8] Sivarajdy et al reported an increasing trend of VRE rate in the bloodstream infections of 6.12% (2018), 13.2% (2019), and 19.2% (2020) at tertiary care hospital in India.[9]

Currently five phenotypes of VRE viz. VanA, VanB, VanC, VanD, and VanE have been identified. [10] Based on MIC values, VanA phenotypes have inducible, high-level resistance to vancomycin with MICs, ≥64 mg/ml and teicoplanin MICs ≥16 mg/ml and VanB isolates have Vancomycin MICs 4 to ≥1,000 mg/ml with teicoplanin MIC ≤4 mg/ml in susceptible ranges. [11] Intrinsic, low-level resistance to vancomycin (MICs, 4 to 32 mg/ml) with susceptibility to teicoplanin is in VanC phenotype found in *E.casseliflavus and E. gallinarum*.[11]

In our study, 50 % of the VRE isolates were *E. faecium* (50%) & Van A phenotype was the commonest phenotype suggested by Vitek 2 system based on MIC values followed by VanB phenotype. Various studies have reported Van A phenotype to be more common. [8, 9, 11]

Various genes such as *vanA*, *vanB*, *vanC1*, *vanC2/C3*, *vanD*, *vanE*, *vanG*, *vanL*, *vanM* and *vanN* have been proven to contribute towards vancomycin resistance in *Enterococci* [9, 11]. Interestingly, van A gene which is plasmid borne is transferable *in vitro* from enterococci to Gram positive organisms like *Staphylococcus aureus*. [12] van A and van B resistance determinants can be transferred from one strain of enterococcus to other as they reside on large mobile elements.[13, 14].

To identify the phenotype, MIC values are required. Kirby Bauer disc diffusion for antimicrobial susceptibility testing has this limitation; Agar dilution method & broth microdilution methods to detect MIC values are cumbersome. Utilization of automated systems reduce time and provide relevant information useful in treatment, earlier infection control measures and surveillance measures. Molecular methods of genotyping of VRE isolates requires dedicated molecular laboratory. In resource limited settings and when time is an important factor, automated identification systems can give a clue towards possible phenotypes so that necessary infection control practices can be implemented as soon as possible.

Cetinkaya et al also pointed out that assessing clinical significance of VRE in routine cultures or to differentiate colonization from infection is not easy, especially in urine and in polymicrobial infection.[11]

The present study has few limitations. Follow up of patients, comorbidities, surveillance cultures, comparison of VRE phenotypes suggested by Vitek 2C automated systems with genotypic methods could have added more information to the study.

Conclusion:

Among the observed VRE isolates, our study found a higher frequency of VRE in *E. faecium* isolates and majority of VRE were of Van A phenotype. In resource limited settings, automated identification systems can help in speciation & give a clue towards possible phenotypes so that necessary infection control practices can be implemented at the earliest.

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