

Prevalence and Distribution of Vancomycin Resistant Enterococci in a Tertiary Care Hospital of Northern India

Unairah Naqash, Asifa Nazir, Rukhsana Taj, Junaid Mehraj Lone

Abstract:

Background: There are no eradication approaches for Vancomycin Resistant Enterococci (VRE) so infection control strategies rely only on screening and isolation of colonised patients.

Objective: To find the prevalence and distribution of Vancomycin Resistant Enterococci (VRE).

Methodology: This was an observational study from a tertiary care hospital which was completed over a period of 18 months.

Results: The prevalence of Enterococcal isolates was 3.9% in our hospital out of which 19.6% were Vancomycin Resistant Enterococci (VRE). Among male subjects the prevalence was much higher (27.5%) in comparison to females (12%) and the difference was found to be statistically significant ($p < 0.001$).

Conclusion: This study emphasizes on the prevalence of vancomycin resistant Enterococci in Tertiary care hospital of Kashmir valley. Enterococcus species has been of particular concern due to their increasing incidence and paucity of drugs available to treat them.

JK-Practitioner 2023;28(3-4):35-40

Introduction

Enterococci are normally considered as bacteria of low pathogenicity, which only infect persons with special immunodeficiency disease.[1] They are most common cause of urinary tract infections, second most common cause of intra-abdominal and intra-pelvic abscesses or post-surgery wound infections and third most common cause of blood stream infections.[2]

The SENTRY Antimicrobial Surveillance Program carried out in the Asia-Pacific (APAC), European, Latin American (LATAM), and North American (NA) regions through 1997 to 2016 found that the overall average frequency of VRE increased from 8% to 15.4% over time in all monitored regions.[3] The prevalence of VRE infections in India is also increasing in the past one decade. Mathur P et al., from New Delhi were the first to report VRE from India in 1999. [4] The reported prevalence from tertiary care hospitals across India ranges from 1.7% to 20%.[5-8] This increase was higher among patients in ICUs, rising from 0.4% to 13.6% in the same time interval. Further, the risk of death from vancomycin resistant Enterococci (VRE) is 75%, compared with 45% for those infected with a susceptible strain.[9] Infection with these organisms causes an estimated 1,300 deaths each year.[10]

The natural ability of *Enterococci* to acquire, accumulate and share extra chromosomal elements encoding virulence traits or antibiotic resistance genes explains their increasing importance as nosocomial pathogens. Acquired resistance to various antimicrobial agents and available antibiotics currently limits the therapeutic options. Furthermore Enterococci have different mechanisms for the transfer of resistance genes, to other pathogenic Gram positive bacteria such as *Staphylococcus aureus* which is very important clinically. The proposed study is an effort to determine the prevalence of Vancomycin Resistant Enterococcal (VRE) infections and also to assess some of the risk factors associated with acquisition of these infections.

Aims and objectives

To find the prevalence and distribution of vancomycin resistant *Enterococci* (VRE).

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Cite This Article as

Naqash U, Nazir A, Taj R, Lone JM. Prevalence and Distribution of Vancomycin Resistant Enterococci in a Tertiary Care Hospital of Northern India. JK Pract 2023;28(3-4):35-40

Full length article available at jkpractitioner.com one month after publication

Keywords

Enterococcus, drug, strain, vancomycin,

Results

A total of 19617 samples were received and processed in our lab out of which 11576 were found to show the growth for various bacteria on culture media. Among the samples, 6003 were isolated from urine, 3944 from pus other body fluids, and 1629 from blood. Out of these 455 Enterococcus were

isolated; 306 from urine, 93 from pus and other body fluids and 56 from blood. The total prevalence of Enterococcal infections was 3.9% and the prevalence among urine, blood and pus and other body fluids was 5.1%, 3.4%, 2.4% respectively. (Table 1)

	No. of samples received (N)	No. of infected samples		No. of samples positive for Enterococcus	
		N	%	N	%
Urine	8519	6003	70.4	306	5.1
Pus and other fluids	6166	3944	64	93	2.4
Blood	4932	1629	33	56	3.4
Total	19617	11576	59	455	3.9

Sample	Total	VRE	VSE	p-value
Urine	306	58 (18.9%)	248 (81.1%)	p = 0.02296 [Chi square = 7.548, Df = 2]
Blood	56	18 (32.1%)	38 (67.9%)	
Pus and other fluids	93	13 (13.9%)	80 (86.1%)	
Total	455	89 (19.5%)	366 (80.5%)	

A total of 455 non-duplicate isolates of Enterococcus were isolated out of which 89 were resistant and 366 were found sensitive depicting the prevalence of vancomycin resistant Enterococcus as 19.5% and vancomycin sensitive Enterococcus as 80.5%. From

Enterococcal isolates the VRE percentage was 18.9 in urine, 32.1% in blood and 13.9 in pus and other body fluids [Table 2]. The difference of VRE isolates from different fluids was found to be statistically significant.

Gender	VRE (n=89)	VSE (n=366)	Total (n=455)	Odds Ratio (95% CI)	P Value
Male	61 (27.5%)	161 (72.5%)	222	2.774 (1.694 – 4.540)	p<0.001 [Chi-square=17.27 df=1]
Females	28 (12.0%)	205 (88.0%)	233		

Table 3 shows the gender distribution of enterococcal isolates. Out of 455 samples, 222 were isolated from males where in 61(27.5%) were VRE and 161(72.5%) were VSE. Among 233 samples from females 28(12.0%) were VRE and 205 (88.0%) were VSE. The difference in percentage of VRE isolates from males and females was found to be statistically significant ($p < 0.001$) and the odds of having more VRE isolates in males was found to be 2.774 (1.694 – 4.540).

Fig. 1: Ward wise Distribution of VRE Isolates

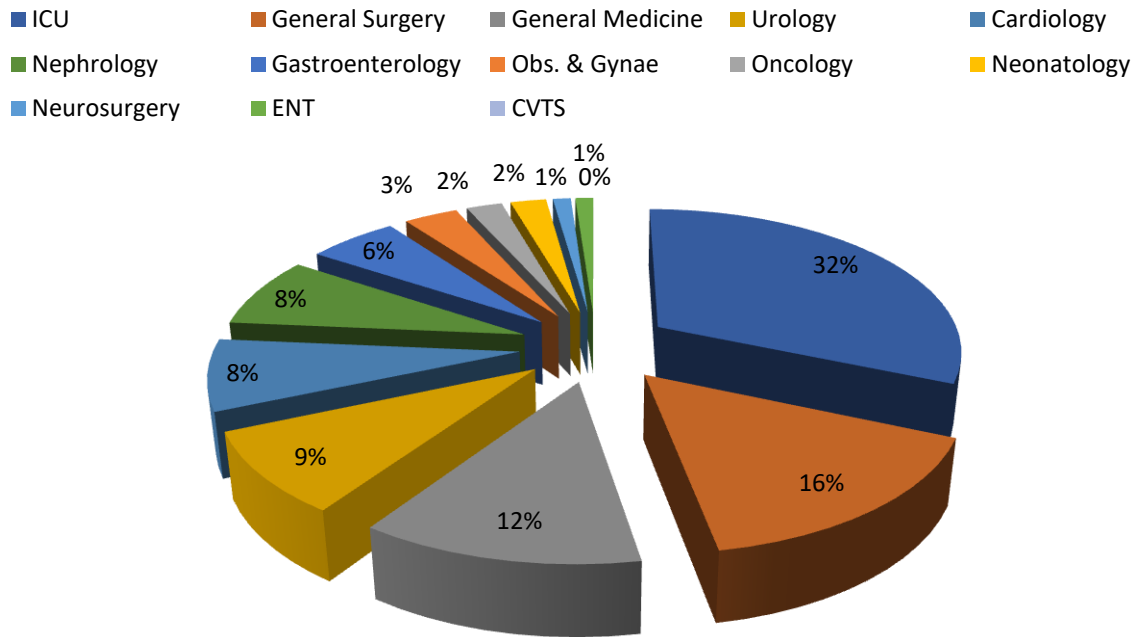


Figure 1 shows the ward wise distribution of VRE isolates wherein VRE were recovered mainly from patients in ICU (32%), followed by general surgery (16%), general medicine (12%), urology (9.0%), cardiology (8%), nephrology (8%) and gastroenterology (6%). Least number of VRE isolates were recovered from neurosurgery and ENTwards.

Table 4: Risk Factors Associated with Vancomycin Resistant Enterococci (multiple responses)

Risk factors	VRE (N=89)	Percentage
IV line	89	100.0%
Antibiotic intake	83	93.3%
Urinary catheter	68	76.4%
Duration of hospital stay >10 days	58	65.2%
Hypertension	21	23.6%
Renal insufficiency	15	16.9%
Steroid intake	9	10.1%
Malignancy	9	10.1%
Diabetes	7	7.9%
Autoimmune disorder	3	3.4%
COPD	3	3.4%

Table 4 depicts the risk factors associated with Vancomycin Resistant Enterococci. Among the 89 patients from whom VRE was isolated, 89(100%) had IV line, 83 (93.2%) had history of antibiotic intake; urinary catheterisation was seen in 68(76.0%) of the patients, 58 of patients (65.1%) had a hospital duration stay of more than 10 days. Co-morbidities like hypertension, diabetes, COPD was seen in 21(23.5%), 7(7.8%) and 03(3.3%) of the patients respectively. Renal insufficiency was seen in 15(16.8%) where as 10.1% (09) had an associated malignant condition and steroidintake.

Discussion

This cross sectional study was carried out in a tertiary care hospital in Kashmir valley in the Post Graduate Department of Microbiology Govt Medical College, Srinagar for a period of eighteen months. Samples

including urine, blood, pus, and other body fluids were processed in the laboratory. Out of the total 19,617 samples received from Oct 2019- May 2021, 11576 were found to show growth on culture media for various bacteria. Enterococcal growth was found

in 455 samples; 366 of which were sensitive and 89 showed resistance to vancomycin. The overall prevalence for Enterococcal infections in our study was found to be 3.9% which is in accordance with studies all over India. **Kalyan R et al (2013) [11]** in their study found the prevalence to be 1.46%, **Kolli HR et al (2016) [12]** reported 4.4%, **Purohit G et al (2017) [2]** reported a prevalence of 5.9%, **Khandelwal N et al. (2020) [13]** reported the prevalence to be 1.5%. Variations in prevalence are attributed to various factors including the type of study, sample size, duration of study

In our study, the data from urine reflected 8519 samples out of which 6003 showed a growth on culture media (hereby referred to as culture positive) for various bacteria. 306 (5.1%) Enterococcal species were isolated out of which 58 were resistant to vancomycin. Pus and other body fluids accounted for 6166 samples with 3944 being determined culture positive for various bacteria; 2.4% of these tabulating to 93 samples were positive for various Enterococcal species out of which 13 were vancomycin resistant. 4932 blood samples were received over the study period out of which 1629 were culture positive. 3.4%. 56 of these were growth positive for *Enterococcus* out of which 18 showed resistance to vancomycin. Our study included the 455 samples from different clinical specimens which showed the growth of *Enterococcus*. Of these 455 isolates, 89 (19.56%) were found to be vancomycin resistant and 366 (80.4%) were sensitive to this glycopeptide. All of 89 VRE isolates had high level vancomycin resistance (MIC > 64 µg/ml) as confirmed by VITEK 2 (bio Merieux). Similar results were reported by **Deshpande VR et al. (2013) [14]**, in their study titled "Prevalence of multidrug resistant Enterococci from a tertiary care hospital in India" and **Oberoi A et al. (2014) [15]**, who in their study found vancomycin resistance in 20% of the isolates. **Arif D et al. (2019) [15]** however in their study reported VRE to be 30% (16/53) which is high as compared to most of the earlier studies from India. From Kashmir valley the earlier studies by **Ahmad J et al. (2015) [17]** and **Manzoor M et al. (2016) [18]** reported a prevalence of 6.5 % and 7% respectively. The above results point towards a steady increase in the prevalence of vancomycin resistant Enterococci in the last decade in India. This increasing trend of VRE bacteremia is a red alert to the clinicians and the infection control practitioners, so that strict antibiotic policies and proper adherence to the infection control practices can be initiated to reduce the VRE rate as was quoted by **Sivaradji M et al. [19]** in their three-year prospective study between October 2017 and September 2020. *Enterococcus* were isolated more from females (51.2%) than males (48.8%) but VRE were isolated more from males (68.5%) which was statistically found significant in our study. Majority of the VRE recovered belonged to the patients in age group of

60-69 years (29.2%), followed by (14.7%) in age group of >50-59 years; the least number of VRE were recovered from patients under age of 0-9 years. Of many risk factors that have been identified with vancomycin resistant infections increasing age has been shown significant in earlier studies done by **Ahmad J et al. (2015) [17]** and **Tripathi A et al. (2015) [20]**. Vancomycin-resistant *Enterococcus* is particularly a problem in the elderly because they are exposed to infections at higher rates in hospital and institutional settings. More over with advancing age infections become a leading cause of morbidity and mortality due to various factors like decreased immunity, presence of chronic co-morbid conditions and alterations in normal physiological organ function which all modifies the severity of infections in elderly patients making them vulnerable to infections. However, both these parameters (age and gender) as per previous study by **Rajkumari N et al. (2014) [21]** were found statistically insignificant. Among the clinical samples, urine had the maximum isolation rate of Enterococci (67.3%) followed by pus and other body fluids (20.4%) and least from blood (12.3%). Results similar to ours were found by **Kolli H Ret al. (2016) [12]** with percentage of 57.4%, 31.5% and 11.1% respectively, **Nautiyal S et al. (2016) [22]** with percentage of 46.0%, 28.3% and 7%, **Manzoor M et al. (2016) [18]** with a percentage of 50.8%, 35.3%, and 13.8 % respectively. **Fawzia A et al. (2017) [23]** with 46.6% isolation rate from urine. Similarly, **Arif D et al. (2019) [16]** reported 66% Enterococcal isolates from urine, 24.4% from pus and 1.8% from blood. **Boccella M et al. (2021) [24]** had reported 32.5% of the isolates from urine. The above data highlights the prevalence of Enterococci in urinary tract infections. There are discrepancies in some studies as by **Geetarani Purohit et al. (2017) [2]** and **Rajkumari N et al. (2014) [21]** where in *Enterococcus* was isolated more from blood than urine. Most of the studies support the same findings as ours the reason being *Enterococcus* is encountered as the most frequent uropathogen, and also being a commensal of GIT, it may be reason for UTI due to the close proximity of anal opening to urethra. Urinary catheterization in some cases may also have contributed to higher isolation of Enterococci from urine. VRE was isolated more from blood (32.1%), followed by urine (18.9%) and (14%) in pus. The isolation of VRE from blood in our study was significant with a p value = 0.02296. In the recent survey (2011– 2014) conducted by the National Healthcare Safety Network (NHSN) at the US Centres for Disease Control and Prevention (CDC), Enterococci ranked first among pathogens associated with central line– associated bloodstream infections (CLABSIs), Enterococcal bloodstream infections (BSI) are associated with a high level of mortality. Most cases of enterococcal BSI are thought to result from translocation of Enterococci from the gut into

the bloodstream. Other routes of infection include along intravenous lines, endocarditis, urinary tract infections and other abscesses. The results of our study are consistent with studies done by **Manzoor M et al. (2016) [18]** and **Chaudhary S et al. (2014) [25]** who reported higher isolation of VRE from blood (34.3%) and (57.1%) respectively. Other studies by **Gupta V et al. (2007) [26]**, **Ghoshal U et al. (2006) [27]**, **Kapoor L et al. (2005) [28]**, **Mathur P et al. (2003) [29]**, also reported a higher isolation of VRE from blood samples. However, some recent studies by **Arif D et al. (2019) [16]** and **Khandelwal N et al. (2020) [13]** reported majority of VRE isolates from urine.

In our study risk factors were accessed for patients from whom VRE were isolated. Most of the patients (31.5%) were admitted in ICU at the time of sampling, followed by patients in surgical and medicine wards (15.7) % and (12.4%) respectively; the next high percentage of patients was seen in urology (9%) followed by nephrology and cardiology wards, each with 7(7.9%) of the total 89 patients 93.2% of the patients with VRE had history of antibiotic administration. The patients had prolonged stay in hospital with 65.1% being admitted for more than 10 days; 100% of patients had IV line, where as urinary catheterization was seen in 76%; 9 out of 89(10%) of the VRE patients were diagnosed with a malignant condition whereas renal insufficiency was seen in 16.8% of the VRE patients. Other co morbid conditions like hypertension, diabetes, and COPD was seen in 21(23.5%), 07(7.8%) and 3(3.3%) respectively. Our findings are consistent with the studies done earlier **Ahmad J et al. (2015) [17]**. In their study they demonstrated a significant relation for antibiotic intake, IV line and urinary catheterization for vancomycin resistant enterococci. **Tripathi A et al. (2015) [20]** found significant association of VRE with renal insufficiency, surgery, hospital stay of >48 hrs, ICU admission and use of antibiotics.

Conclusion

The prevalence of Enterococcal isolates in our study was found to be 3.9% which was comparable to other studies. The VRE isolates were more common in males and in blood samples. As there are no eradication approaches for VRE so infection control strategies rely only on screening and isolation of colonised patients. Also antibiotic stewardship programs that limit the use of cephalosporins, antibiotics against anaerobes, vancomycin and broad spectrum antibiotics can play an essential role in preventing the emergence and spread of this pathogen.

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