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Pattern and extent of Vancomycin resistance in a tertiary care teaching center

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Abstract
Context: Emerging resistance to Vancomycin is a matter of serious concern as it is the drug of choice for the management of infections with multidrug resistant gram positive bacterial strains. Substantial proportions of bacterial strains are developing resistance to Vancomycin.
Aim: To study the pattern and extent of Vancomycin resistance among different bacterial isolates obtained from blood specimens.
Method and Material: A cross sectional observational study was conducted in a tertiary care teaching hospital of central India. The data of Vancomycin resistance was obtained from culture and sensitivity reports from Department of Microbiology.
Statistical analysis used: Ninety five percent Confidence interval of proportion of Vancomycin resistant isolates was calculated.
Result: Blood culture positivity rate was found to be 39.4%. The isolates having growth of gram positive bacteria were found to be 16.6% of all the positive growth. The most common gram positive bacteria were staphylococcus. The resistance to Vancomycin was found to be 24.5% among gram positive bacteria.
Conclusion: The information and data regarding pattern of Vancomycin resistance may be helpful to solve the problem of emerging Vancomycin resistance. The reduction in the indiscriminate use of Vancomycin is an important approach to impede its resistance.

Keywords: Vancomycin, Vancomycin resistant Staphylococcus aureus, Vancomycin resistant Enterococcus, Blood steam infections.

1. Introduction
Vancomycin, a glycopeptide antibiotic was discovered in 1956. Vancomycin is produced by Streptococcus orientalis. It is one of the most effective drug against resistant gram positive bacteria particularly MRSA (Methicillin resistance Staphylococcus aureus). Its microbial spectrum includes gram positive bacteria, Neisseria, Clostridia and Diphtheroids, but it is inherently inactive against gram negative bacteria. It has unique significance as it is highly active against MRSA, Streptococcus viridians, Enterococcus and Clostridium difficile. It is considered as reserve drug for multidrug resistant gram positive bacteria. But increasing indiscriminate use of Vancomycin lead to emergence of Vancomycin resistant staphylococcus aureus (VRSA) and vancomycin resistant Enterococcus (VRE) [1, 2].
Vancomycin has unique mechanism of action. It inhibits bacterial cell wall synthesis. It get attach to peptidoglycan unit at terminal dipeptide D-alanyl-D-alanine of cell wall precursor units so that assembly and cross linking of units cannot take place. It involves binding of the bulky inhibitor to the substrate outside the membrane so that the active sites of two enzymes cannot align themselves correctly. The acquisition of resistance to Vancomycin more is difficult than that to the majority of the other antibiotics. In spite of this the resistance to Vancomycin is increasing day by day [3]. In fact, some case repots had found VRSA in absence of Vancomycin exposure [4]. The increasing prevalence of VRSA is threat to medical fraternity. Sepsis and other infection caused by Vancomycin resistance are very difficult to manage and as there are few options left available to deal with VRSA [5]. Therefore, present study was conducted to determine the pattern and extent of Vancomycin resistance.

2. Method and Material

A cross sectional observational study was conducted in a tertiary care teaching center of central India. Blood specimens routinely submitted for cultures and sensitivity during the period of September to December 2013 to the microbiology laboratory of the hospital were included in the study. The antibiotic resistance patterns of the organisms were performed by Kirby- Bauer's disk diffusion method on Mueller Hinton agar plates by Department of Microbiology. We collected the data regarding Vancomycin resistance and sensitivity from laboratory records. The data obtained were analyzed and results obtained were expressed by descriptive statistics. Ninety five percent confidence interval of proportion of Vancomycin resistant strains was calculated by online available website http://www.graphpad.com/.

3. Result

Total 1855 blood specimens were received during period of September 2013 to December 2013, out of these 732 turned out to be positive while 1123 found to be negative for growth of bacteria. The positivity rate was found to be 39.4%. Out of 732 isolates, gram negative isolates accounts for 610 (83.33%) while gram positive strains were found to be 122 (16.66%). The gram positive bacteria isolates includes Staphylococcus 87 (11.8%), Coagulase negative staphylococcus (CONS) 20 (2.7%), and Streptococcus 15 (2%).

Among the 87 Staphylococcal isolates 65 found to be sensitive while 22 found to be resistant to Vancomycin. Around 25.2% Staphylococcal isolates were Vancomycin resistant with 95% confidence interval of (0.17 to 0.36). And among the 20 CONS isolates 16 found to be sensitive while 4 found to be resistant to Vancomycin. Around 20% CONS isolates were Vancomycin resistant with 95% confidence interval of (0.09 to 0.49). In the same way, among the 15 streptococcal isolates 11 found to be sensitive while 4 found to be resistant to Vancomycin. Around 26.6% Streptococcal isolates were Vancomycin resistant with 95% confidence interval of (0.08 to 0.55). Out of all 122 gram positive isolates 92 found to be sensitive while 30 found to be resistant to Vancomycin. Total 24.5% gram positive isolates were Vancomycin resistant with 95% confidence interval of (0.18 to 0.33).

4. Discussion

Vancomycin resistance was first reported in 1988 among Enterococcal strains. These Vancomycin resistant organisms rapidly spread to various intensive care units of every corner of world. In 1992, acquisition of Vancomycin resistance by conjugative transfer of the Vancomycin resistance gene VanA from enterococci to S. aureus was demonstrated [4]. However, the first case of Vancomycin Resistant Staphylococcus Aureus (VRSA) was detected in 1996 from Japan. Vancomycin resistance is acquired by mutation that causes increase in accumulation of excess amounts of peptidoglycan which results in thickening of cell wall. This seems to be a common mechanism responsible for resistance among all VRSA strains [6].

The prevalence of Vancomycin resistant bacteria is subjected to regional, periodic and racial variation. A study conducted in India has identified that the prevalence of vancomycin resistance among the staphylococcus was 11.1% in 2010 [7]. Baky *et al* (2014) have reported that 1.6% of staphylococcal isolates were resistant to Vancomycin [8]. According to Furtado *et al* the incidence of Vancomycin resistance was 15.8% in 2002 [9]. The prevalence of Vancomycin resistance among enterococci species in community-hospitals and medical centers was found to be 16% and 21% respectively [10]. In a Nigerian study conducted in 2013, 19 (5.4%) isolates were Vancomycin resistant out of 355 Staphylococcus aureus isolates [11]. In a study conducted by Tabatabaei *et al* (2012), it was observed that the 16.9% of enterococci isolated from patients were resistant to Vancomycin [12]. And in our study, we have found that resistance to Vancomycin was around 24.5% with the 95% confidence interval of 0.18 to 0.33. The prevalence of resistance detected in our region is considerably high as compared to other studies.

There are some limitations of in our study; it is a single centric observational study and there is absence of isolation and confirmation of Vancomycin resistant isolates. Multi-centric studies are required to know the prevalence of Vancomycin resistance and to provide strength for this evidence.

Table 1: The number, percentage and confidence interval of resistance to Vancomycin in gram positive bacteria

Resistance Pattern To Vancomycin					
Bacteria	**No. of total isolates**	**No. of sensitive isolates**	**No. of resistant isolates**	**Percentage of resistant isolate**	**95% Confidence interval**
Staphylococcus	87	65	22	25.2%	0.17 to 0.36
CONS	20	16	4	20.0%	0.09 to 0.49
Streptococcus	15	11	4	26.6%	0.08 to 0.55
Total	122	92	30	24.5%	0.18 to 0.33

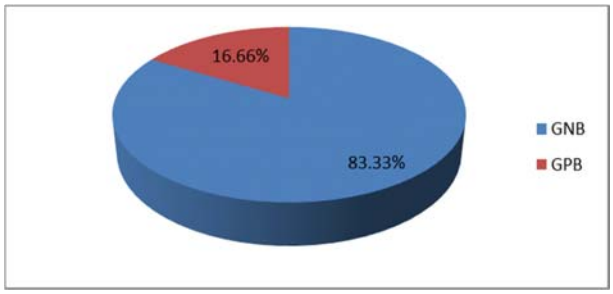

Fig 1: Proportion of Gram positive bacteria (GPB) and Gran negative bacteria (GNB)

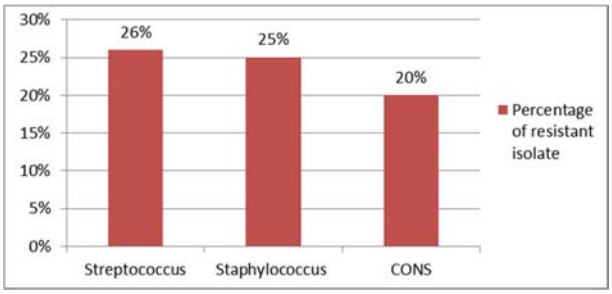

Fig 2: Resistance pattern to Vancomycin among Gram positive bacteria

5. Conclusion

Better understanding of these issues can play a key role in preventing spread of Vancomycin resistance. The steps must be taken in order to prevent transmission of Vancomycin resistance among the gram positive bacteria. Prompt identification of patients harboring VRSA, VISA or hVISA as well as isolation and adherence to infection control measures are paramount in controlling the dissemination of these pathogens. Substantial numbers of bacterial strains are developing resistance to Vancomycin. The antimicrobial agent like Vancomycin is precious and finite resources, we must use this rationally and judiciously to maintain its effectiveness. If no action is taken today; we will lose the effectiveness of this novel antimicrobial agent in near future.

6. Conflict of Interest: The authors declare that they have no conflict of interest.

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