Screening and detection of heterogenous vancomycin intermediate \textit{Staphylococcus aureus} in Hospital Kuala Lumpur Malaysia, using the glycopeptide resistance detection Etest and population analysis profiling

Siti Roszlawati Ramli,1,2 Hui-min Neoh,3 Muhammad Nazri Aziz,4 Salasawati Hussin1

1Department of Microbiology and Immunology, University Kebangsaan Malaysia Medical Centre; 2Institute for Medical Research, MalaysiaJalan Pahang; 3UKM Medical Molecular Biology Institute,University Kebangsaan Malaysia; 4Department of Pathology,Hospital Kuala Lumpur, Malaysia

Abstract

In a 3-month study done in Hospital Kuala Lumpur (HKL), 7 out of 320 methicillin resistant \textit{Staphylococcus aureus} isolates were confirmed as heterogenous vancomycin intermediate \textit{S. aureus} (hVISA) using the glycopeptide resistance detection e-test and population analysis, giving a prevalence rate of 2.19%. This is the first report of hVISA in Malaysia.

Introduction

Heterogenous vancomycin intermediate \textit{Staphylococcus aureus} (hVISA) strains have been reported as indicators for reduced vancomycin susceptibility in \textit{S. aureus},1 and various studies associated its presence with vancomycin treatment failure.2 It has been shown that methicillin resistant \textit{S. aureus} (MRSA) has the propensity to evolve into hVISA phenotype during \textit{in vitro} exposure to sub-inhibitory concentrations of vancomycin.3 During the last decade, hVISAs had been isolated in many countries including those in South East Asia;4 nevertheless, in our knowledge, its emergence has not been reported in Malaysia. As a pilot study, we investigated the prevalence of hVISA among MRSA strains isolated at Hospital Kuala Lumpur (HKL) in a 3-month period and determined factors associated with its infections.

Case Report

Hospital Kuala Lumpur is the largest hospital in Malaysia with the highest MRSA burden in the country.1 In this hospital, vancomycin is used as the standard first line treatment for MRSA infection; however, recently, its efficacy has been a subject of discussion due to several anecdotal vancomycin treatment failure cases in Hospital Kuala Lumpur. We also wondered if some of the MRSA isolates in the hospital were actually hVISAs with reduced susceptibilities to vancomycin that could not be detected by routine microbiological tests used in our hospital diagnostic laboratory. To investigate this, from 25th February to 25th May 2009, we collected a total of 320 index MRSA isolates (first MRSA isolated from the corresponding patients) and established them as strains for vancomycin resistance testing. As it is cost, time and labor consuming to perform vancomycin population analysis6 on all 320 strains to test for heterogenous vancomycin resistance, strains were first screened for the phenotype using Glycopeptide Resistance Detection (GRD) Etest antibiotic strips (AB BIODISK, Sweden).7 After GRD screening, a total of 8 strains were defined as presumptive hVISA, no VISA strain was detected. Following that, to confirm the results of the GRD screening, the 8 presumptive hVISAs were subjected to vancomycin population analysis. Interestingly, area under the curve (AUC) analyses8 of the strains’ population analysis profiles confirmed that 7 out of the 8 tested strains were hVISA (Table 1), giving a prevalence rate of 2.19%.

Discussion

All hVISA strains isolated in this study were hospital acquired as they were isolated from their corresponding patients after 48 hours of hospital admission. To determine factors associated with the 7 hVISA infections, demographic data of all corresponding patients of each index MRSA isolate were retrieved from medical records. Medical history of each patient such as diabetes mellitus, renal failure, malignancy, together with prescription history of vancomycin and beta-lactam antibiotics (as these were the only classes of antibiotics prescribed to the corresponding patients of the study isolates during this investigation), length of hospitalization and intensive care unit (ICU) admission were recorded. Continuous variables were then assessed by independent samples t-test, while categorical variables were analyzed using Pearson’s Chi-square. Calculations were performed using Statistical Package for Social Science (SPSS) 12.0 (SPSS Inc., Chicago, USA) where a P-value of <0.05 was considered as significant. After performing multivariate linear regression, we found that ICU admission (P=0.004), hospitalization of more than 14 days (P=0.014) and vancomycin administration of more than 7 days (P<0.016) were independent factors associated with hVISA infections in our group of patients. Our findings were in line with those of Charles et al. in 2004, where hVISA/VISA infections were found to be associated with longer antibiotic treatment periods and longer hospitalization.9 In a separate report, ICU admission was also stated as a significant associated factor for hVISA infections.10 It seems that patients who are severely ill, hospitalized for long durations with ICU admissions might have a higher chance of developing hVISA infections. As many patients in HKL fulfill some or all of the above criteria, taking it together, we suspect that the prevalence of hVISA in HKL might be high; however, these strains are not being actively detected by

Acknowledgements: this project was funded by UKMMC (FF-085-2009). The authors wish to thank the Director General of Health, Ministry of Health, Malaysia, for permission to publish this Paper; and Prof. Dr. Keichi Hiramatsu of Juntendo University, Japan, for the generous gift of reference strains.

Contributions: SRR, study concept and design, data acquisition, methods, and manuscript preparation; HN, study concept and design, and data acquisition; SH, study design, data analysis and assisted with manuscript preparation.

Conflict of interest: all other authors report no conflicts of interest.

Received for publication: 22 October 2011. Revision received: 19 December 2011. Accepted for publication: 8 January 2012

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

Correspondence: Hui-min Neoh, UKM Medical Molecular Biology Institute (UMBI), UKM Medical Centre, 56000 Kuala Lumpur, Malaysia. Tel. +603.9171.8459 - Fax: +60.3.9171.7185. E-mail: hui-min@ppukm.ukm.my

Key words: heterogenous vancomycin intermediate \textit{Staphylococcus aureus} (hVISA), Hospital Kuala Lumpur.
We found the GRD test useful for hVISA in this hospital. It might be even higher in hospitals where most hospitalized patients are severely ill with long hospitalization durations. Once identified as hVISA infected, optimal treatment could be prescribed to the corresponding patient to prevent vancomycin treatment failure, thereby increasing the chance of a good clinical outcome for the patient.

**Conclusions**

This is the first report of hVISA in Malaysia. As the strains used in this study were collected in a short span of 3 months, and that vancomycin treatment failure is on the rise in HKL, we suspect that the actual prevalence of hVISA in this hospital might be even higher. We found the GRD test useful for hVISA screening, nevertheless PAP-AUC analysis still remains the gold standard for hVISA confirmation. A more comprehensive, case control study involving major hospitals in the country would be important to better understand the significance and distribution of hVISA in Malaysian hospitals.

**References**


