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Novel substitution of glutamine with lysine at position 16 of Hepatitis B surface antigen associated with diagnostic and immune escape

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Hepatitis B surface mutants are capable of infecting both vaccinated and unvaccinated populations, putting the whole population at risk. Clinically important hepatitis B surface antigen mutants have been reported in all genotypes [1]. Therefore, understanding the diversity of such mutations will be useful in designing a diagnostic assay and in the prevention and treatment of occult hepatitis B infection. However, molecular characterization of immune and diagnostic escape hepatitis B strains in Southeast Asia has not been extensively performed. Hence, this was the aim of the present study. One thousand serum samples were collected from blood donors and vaccinees. All samples were tested for hepatitis B surface antigen and hepatitis B core antibodies using an enzyme-linked immunosorbent assay. The results showed that 5.5% (55/1000) of samples were core antibody-positive but none of the samples were surface antigen-positive. Nested polymerase chain reaction was done for all hepatitis B core antibody-positive samples and were all found to be HBV DNA positive. The amplified S gene fragment was purified and sequenced, after which mutation analysis was done using BioEdit v7.2.0. The most prevalent mutation found in this Malaysian isolate was substitution of glutamine at position 16 with lysine, different from the previously reported G145R, yet hepatitis B surface antigen could not be detected using serology. Diagnostic escape mutants might be a result of posttranscriptional effect of the mutation on hepatitis B surface antigen expression [2, 3]. This would reduce the effectiveness of diagnostics and vaccine-induced immunity, leading to escape of neutralization by the current vaccine and occult infection [4]. In conclusion, most of the mutations found in this study were outside the “a” determinant and major hydrophilic regions of the S gene and associated with vaccine and diagnostic escape hepatitis B virus infection. This study suggests that mutation outside the “a” determinant region may play a major role in hepatitis B surface antigen detection and vaccine response.

Keywords: Hepatitis B Surface Antigen, Escape Mutations, Polymerase Chain Reaction, Blood Donors, Vaccinees

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