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DETECTION OF HEPATITIS B VIRUS GENOTYPES A AND D ASSOCIATED WITH LIVER DISEASE IN A TERTIARY HOSPITAL

By

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DECLARATION

"I hereby declare that this thesis is my original work and has not been submitted previously or currently for any other degree at UiTM or any other institutions."

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ABSTRACT

DETECTION OF HEPATITIS B GENOTYPES A AND D ASSOCIATED WITH LIVER DISEASE IN A TERTIARY HOSPITAL

Today, hepatitis B virus (HBV) infection remains as the main etiology of liver disease worldwide. Presently, there are 10 different HBV genotypes (A to J) established with distinct geographical distribution and a discrete clinical outcome respectively. Generally, there are two genotypes predominantly high in prevalence in certain regions. Predominant genotypes in Malaysia are genotype B and C. Currently, studies on other genotypes and their association with liver disease are not widely known. This is a preliminary study which is designed to detect hepatitis B genotype A and D in a positive HBV infected patients diagnosed with liver disease among Malaysian population. This study also aimed to find the correlation between socio-demographic data and viral loads with HBV infection and towards contribution to the progression of liver disease. In this study, 60 serum samples collected were identified positive with HBV infection between March to April 2015 from the Kuala Lumpur Hospital were examined. However, only 35 samples were successfully genotyped. The study involved the DNA extraction process by using QIAamp® DNA Blood Mini Kit. Following, extracted DNA were analysed by real-time polymerase chain reaction (qPCR) where QuantiFast® SYBR® Green chemistry was used. Genotype A and D were detected, and the results obtained were analysed statistically. Generally, socio-demographic data might have influence on HBV infection and disease progression. However, all the statistical analysis revealed that there is no significant association between HBV genotype A and D with age, race and gender concerning influences in advancement of liver disease. HBV viral loads also insignificantly associated with HBV genotypes A and D. This study suggested that the detection of genotype A and D will shed lights on new data for hepatitis B genotypes other than B and C. The outcomes can be referred as a new insight on HBV genotypes associated with liver disease patients in Malaysia. Further studies are required with a bigger sample size so that better understanding regarding different HBV genotypes can be achieved.

Keywords: hepatitis B virus (HBV), genotype A, genotype D, liver disease, real-time polymerase chain reaction (qPCR).

CHAPTER 1

INTRODUCTION

1.1. Study Background

The human hepatitis B virus (HBV) is recognised as a small enveloped DNA virus that can cause both acute and chronic hepatitis (Hadi, Mustafa, & Chee, 2014). Studies reported that nearly hundreds million people chronically infected with this human-only reservoir pathogen (Hwang & Cheung, 2011). Hepatitis B could possibly causes variable spectrum of liver diseases ranging from an asymptomatic to severe (Tanwar & Dusheiko, 2012). Liver diseases that are associated with HBV including liver failure, cirrhosis and hepatocellular carcinoma (HCC) reported by Malaysian Oncological Society to have caused over 1 million deaths occurs annually (Ismail, 2011). Roughly, up to 40% chronic HBV patients will develop cirrhosis and HCC in their lifetime (Hwang & Cheung, 2011). In Malaysia, HBV is known as the main etiological agent causing HCC, whereas HCC ranked 7 as a cancer-related death (Suppiah, Mohd Zain, Haji Nawi, Bahari, & Saat, 2014).

Globally, hepatitis B endemicity are respectively divided into three groups of high (>8%), intermediate (2 - 7%) and low (<2%) endemicity areas (Hudu, Malik, & Niazlin, 2013). In the past, Asia Pacific was once categorised as a high endemic region (Hudu *et al.*, 2013). Fortunately now it is considered as an intermediate endemic region (Hudu *et al.*, 2013). In the meantime, Malaysia also make a turn from being an intermediate endemic area into low endemic area due to the effective implementation of hepatitis B vaccine (Hudu *et al.*, 2013). In present, only a few countries like Vietnam and Laos remain in high category in the region with a prevalence of 8.8% and 8.7%, individually (Hudu *et al.*, 2013).

Remains as a worldwide public health problem, HBV infection is well known to have two types of transmission which includes vertical and horizontal (Hwang & Cheung, 2011). In highly endemic areas, the common mode of transmission is either vertical or horizontal early in life, consequential in a high chronicity rate (Tanwar &