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ISID Small Grant Program Report

Molecular Epidemiology of Hepatitis B Virus in Minangkabau Ethnic Group of West Sumatera, Indonesia

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Background

Hepatitis B virus (HBV) infection is associated with a diverse clinical spectrum of liver damage ranging from asymptomatic carriers (AC), chronic hepatitis (CH), liver cirrhosis (LC), and hepatocellular carcinoma (HCC). WHO estimated about 2 billion people worldwide have been infected by the virus and 350 million people live with chronic HBV infection. Indonesia was reported to have intermediate to high endemicity [1].

Currently there are eight established (A–H) and two putative (I–J) HBV genotypes with distinct geographical distributions. Genotype B and C are highly endemic in East Asia including Indonesia. There are four HBV genotypes found in Indonesia (A–D), where genotype B has been found as the major genotype [1–5]. HBV genotypes have been reported to be related with severity of liver disease. For example, genotype C has higher disease-inducing capacity compared to genotype B in East Asian countries through high incidence of core promoter mutation [6–8].

Minangkabau is one of the four major ethnic groups in Indonesia with population of approximately 5.3 million. They originally reside in the West Sumatera province. Padang is the capital city of West Sumatera with a population of over 833,000 (census 2010). A preliminary study on HBV molecular epidemiology of Minangkabau ethnic group prevailed different prevalence of HBV genotypes compare to Indonesian population in general [4]. This study aimed to further analyze the prevalence of HBV genotype in Padang population and specifically Minangkabau ethnic group.

Materials and Methods

Blood samples were collected from M. Djamil Hospital Padang, West Sumatera and Blood Transfusion Unit, Red Cross Padang, West Sumatera. The samples were taken from 147 blood donors, and 42 liver disease patients comprised of 16 CH, 22 LC, and 4 HCC patients. Informed consent was obtained from each participant. HBsAg test for all samples were performed by a commercially available ELISA kit (Abbott Laboratories, Chicago, IL). HBV DNA was extracted from 200 µL plasma using the QIAamp DNA blood mini kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. HBV genotype, subgenotype and BCP double mutation were determined as previously described [5,9]. Statistical analyses were performed using SPSS 17.0 software for Windows (SPSS Inc., Chicago, IL, USA) and $P < 0.05$ was considered significant.

Results and Discussion

The study included a total of 189 samples with positive HBsAg test, 165 males and 24 females. The mean age of subject was 37.5 ± 11.6 years old. Of 189 samples, 140 (74.1%) and 99 (52.4%) samples were positive for genotyping and subgenotyping, respectively. Genotype C was found in 84 (60.0%) samples, genotype B was found in 49 (35.0%) samples, and mix genotypes B and C was found in 7 (5.0%) samples. Based on its ethnicity, the samples were divided into two groups: the Minangkabau ethnic group and other ethnics group, which includes the Javanese, Sundanese, Batak, and other Sumateranese ethnics. From 189 samples, 98 (70.0%) samples belong to Minangkabau ethnic group. Male/female ratio and mean age of the two groups are similar. Ratio of genotype B and C and mix genotype of B/C for Minangkabau ethnic group and other ethnics group were 19.4% : 77.6% : 3.1% and 71.4% : 19.1% : 9.5%, respectively. The genotype distribution between the two groups were significantly different ($P < 0.001$). The major subgenotypes in the samples from Padang were C1 (62.6%)

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followed by B3 (24.2%) and B7 (4.0%). If we compared the HBV genotype prevalence between Minangkabau and other ethnic groups, it was found that in the Minangkabau ethnic group the subgenotype C1 (76.4%) was more dominant than subgenotype B3 (18.1%), while in the other ethnic group the major subgenotype was B3 (40.7%) followed by subgenotypes C1 (25.9%) and B7 (14.8%).

The present study showed the difference of HBV genotype and subgenotype distribution in Minangkabau ethnic compared to those in Indonesian population in general [4,5]. HBV genotype C with majority of subgenotype C1 was found as the major HBV genotype in Padang, specifically in Minangkabau ethnic group. Although another study reported that HBV genotype C was also prevalent in the eastern part of Indonesia (Moluccas and Papua), the main subgenotypes in this area were C5 and C6 [4, 10], different with genotype C found in Minangkabau ethnic. In other countries, HBV genotype C is more prevalent in East Asia, such as in China and Taiwan. Longitudinal cohort studies in Taiwan demonstrated that HBV genotype C is an independent risk factor for HCC development and is associated with a higher risk of reactivation of hepatitis B and progression to cirrhosis than HBV genotype B [11-13]. Longitudinal cohort study needs to be performed in order to investigate the association of HBV genotype C and risk of HCC in Minangkabau population.

Conclusions

The HBV genotype distribution in the population of Minangkabau ethnic is different than that of other Indonesian HBV carrier in general. Minangkabau ethnic group has higher prevalence of HBV genotype C than other ethnic groups (77.6% vs 19.1%). Subgenotype C1 and B3 are the major subgenotypes found in this ethnic group. These preliminary results indicate that the Minangkabau ethnic group may be at higher risk of developing severe liver disease.

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