

CLINICAL STUDIES

Genotype diversity of hepatitis C virus (HCV) in HCV-associated liver disease patients in Indonesia

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Abstract

Background: Hepatitis C virus (HCV) genotype distribution in Indonesia has been reported. However, the identification of HCV genotype was based on 5'-UTR or NS5B sequence. **Aims:** This study was aimed to observe HCV core sequence variation among HCV-associated liver disease patients in Jakarta, and to analyse the HCV genotype diversity based on the core sequence. **Methods:** Sixty-eight chronic hepatitis (CH), 48 liver cirrhosis (LC) and 34 hepatocellular carcinoma (HCC) were included in this study. HCV core variation was analysed by direct sequencing. **Results:** Alignment of HCV core sequences demonstrated that the core sequence was relatively varied among the genotype. Indeed, 237 bases of the core sequence could classify the HCV subtype; however, 236 bases failed to differentiate several subtypes. Based on 237 bases of the core sequences, the HCV strains were classified into genotypes 1 (subtypes 1a, 1b and 1c), 2 (subtypes 2a, 2e and 2f) and 3 (subtypes 3a and 3k). The HCV 1b (47.3%) was the most prevalent, followed by subtypes 1c (18.7%), 3k (10.7%), 2a (10.0%), 1a (6.7%), 2e (5.3%), 2f (0.7%) and 3a (0.7%). HCV 1b was the most common in all patients, and the prevalence increased with the severity of liver disease (36.8% in CH, 54.2% in LC and 58.8% in HCC). These results were similar to a previous report based on NS5B sequence analysis. **Conclusion:** Hepatitis C virus core sequence (237 bases) could identify the HCV subtype and the prevalence of HCV subtype based on core sequence was similar to those based on the NS5B region.

Hepatitis C virus (HCV) infection is known to be a major contributor to chronic liver diseases including chronic hepatitis, liver cirrhosis (LC) and hepatocellular carcinoma (HCC). Variability of the RNA genome of HCV has made it possible to distinguish six genotypes and over 70 subtypes (1). Relatively well-conserved regions of the genome (5'-UTR, C/E1 and NS5B) have been used as the basis for the HCV classification (1, 2). The varied genotypes differ in distribution both by geographical region and by mode of transmission. Based on NS5B and 5'-UTR sequences, we demonstrated previously that the genotypes 1 (subtype 1a, 1b and 1c), 2 (mainly subtype 2a) and 3 (mainly subtype 3k) are found among blood donors and HCV-associated liver disease patients in Indonesia (3), similar to others' observations (4–6).

The current standard treatment for patients with chronic hepatitis C consists of pegylated α interferon (Peg-IFN) in combination with the nucleoside analogue ribavirin for 24–48 weeks, and leads to a sustained

virological response in 54–56% of cases (7, 8). Sustained virological response is defined as undetectable HCV RNA by a sensitive assay (lower detection limit of < 50 IU/ml) at the end of a 24-week follow-up period after the end of treatment. Patients who do not achieve a sustained virological response may be found to be HCV RNA negative during therapy but may relapse thereafter, or may be non-responders who have detectable HCV RNA throughout the treatment period. Virological response rates have been shown to vary with host and viral factors such as age, weight, sex, race, liver enzymes and stage of fibrosis, HCV genotype and HCV RNA concentration at baseline (7–11). In addition, each genotype also displays particular features such as resistance to Peg-IFN and ribavirin combination treatment, for example, genotype 1-infected patients respond less efficiently to therapy than those infected with genotype 2 and 3 viruses (7).

Previous studies have reported that, especially in HCV genotype 1b, polymorphisms of amino acid (aa) no. 70 of