The molecular epidemiological study of hepatitis B virus (HBV) in Indonesia is still limited. This study was aimed to identify the prevalence of HBV pre-S deletion/insertion mutations, and to assess the association of pre-S deletion mutation with liver disease progression in Indonesia. Pre-S mutations were identified by direct sequencing. Of the 265 subjects, 32 samples (12.1%) harbored pre-S deletion/insertion mutations. The prevalence of those pre-S mutations was 2.7% (2/75), 12.9% (8/62), 16.7% (11/66), and 17.7% (11/62) in asymptomatic carrier, chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma groups, respectively. Statistical analysis showed significant difference among them ($P = 0.024$). In HBV genotype B (HBV/B), pre-S1, pre-S1/S2, and pre-S2 deletion mutations were detected respectively in 3 (17.6%), 4 (23.5%), and 9 (52.9%) of 17 samples. On the other hand, in HBV/C, 12 of 15 samples (80.0%) showed a pre-S2 deletion mutation, and only 2 samples (13.3%) demonstrated a pre-S1/S2 deletion mutation. These results suggest that in HBV/B deletion mutation tends to occur in pre-S1 or pre-S1/S2 region, while in HBV/C the deletion mutation usually occurs in the pre-S2 region. Analysis of complete genome of four viruses confirmed that 3 isolates were classified into HBV/B3, and 1 isolate was HBV/C1. However, SimPlot and BootScan analyses showed that isolate 08.10.002 was an intragenotypic recombinant between HBV/B3 and HBV/B4. As conclusion, the prevalence of HBV pre-S mutations was relatively low in Indonesian patients compared to those from Taiwan, Japan, and other Asian countries. There was a weak association between pre-S deletion mutation and progressive liver disease. **J. Med. Virol. 83:1717–1726, 2011.** © 2011 Wiley-Liss, Inc.

**KEY WORDS:** hepatitis B virus; pre-S deletion mutation; liver disease; Indonesia

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**INTRODUCTION**

Hepatitis B virus (HBV) infection is a major health problem leading to significant morbidity and mortality worldwide. Approximately, two billion people in the world have been infected by HBV [Zuckerman and Zuckerman, 2000]. Indonesia has a moderate-to-high endemcity of HBV infection [Sastrosoewignjo et al., 1991], perhaps due to the lack of proper health facilities, poor economical status, less public awareness, or incomplete vaccination. The majority of acute HBV infections are self-limiting, whereas chronic HBV infections can lead to severe liver disease and even liver cancer. The natural history of HBV infection is variable and depends on factors such as age at infection, viral load, and host immune response. The development of chronic infection is more common in infants and young children, and severe liver disease is more likely to occur in chronic HBV carriers. Therefore, understanding the molecular epidemiology of HBV in Indonesia is crucial for developing effective prevention and control strategies.