3936701 SIMI/M : MAJOR : MICROBIOLOGY ; M.Sc (MICROBIOLOGY)
KEY WORDS : HEPATITIS B VIRUS/ MUTATION / CORE PROMOTER PRECORE GENE / HEPATITIS B e ANTIGEN

KRIANGSAK RUCHUSATSAWAT : ANALYSIS OF MUTATIONS IN THE *S* GENE, CORE PROMOTER AND PRECORE GENE OF THE THAI ISOLATES OF HEPATITIS B VIRUS. THESIS ADVISORS : SIRIRURG SONGSIVILAI, M.D., Ph.D., TARARAJ DHARAKUL, M.D., Ph.D. 114 P. ISBN 974-664-060-7.

Hepatitis B virus is a major causative agent of hepatitis that can cause life-long chronic infection, cirrhosis, liver cancer, liver failure and death. Detection of viral and immunological markers are useful in the diagnosis and monitoring of the infection. The presence of HBeAg is one indicator of active viral replication, whereas anti-HBe antibody is believed to be a marker of recovery. However, some patients may have active viral infection in the absence of HBeAg which is postulated to be due to mutation in the genes encoding the HBc/HBe antigen.

In order to investigate the prevalence and importance of gene mutations in this region, nucleotide sequences were obtained from 61 chronic hepatitis patients. Of these 61 samples, genotype A, B and C were found in 1.6, 29.5 and 68.9%, respectively. Mutations in the core promoter region at position 1762 (A1762T) and 1764 (G1764A) were found in 33 patients (54.1%), in which 13 (39.4%) were HBeAg-negative and the other 20 (60.6%) were HBeAg-positive.

In the precore region, the classical mutation at position 1896 (G1896A) was found in 19 (31.1%) patients in which 17 (89.5%) were HBeAg-negative and the other 2 (10.5%) were HBeAg-positive. There is a significant correlation between HBeAg-negative status and mutation at G1896A ($p< 0.0001$). The mixed infection with wild type and mutant virus (G1896r) were found in 7 (11.5%) patients in which 6 (85.7%) were HBeAg-positive and one (14.3%) was HBeAg-negative.

In addition, the nucleotide sequences in the *S* gene were obtained from 10 patients; 8 were from genotype C, 2 were from genotype B. The sequences were used to design a synthetic peptide spanning the 'a' determinant of the HBsAg. However, attempts were unsuccessful in using this peptide as an immunodiagnostic reagent.

In the situation in Thailand where about almost 50 % of HBV infected patients had mutant viruses, HBeAg in the blood may not directly correlate with the absence of active hepatitis B infection.