

Seroprevalence of HBV Infection and Vaccine Escape Mutants: 22 years after Infant HBV vaccination in Iran

Mohammad Reza Aghasadeghi¹, Arezoo Aghakhani², Setareh Mamishi³, Mahmood Nabavi⁴, Sepehr Soleymani¹, Mohammad-Taghi Haghi Ashtiani⁵, Mohammad Banifazi⁶, Rouhollah Vahabpour¹, Fatemeh Motevalli¹ and Amitis Ramezani²

1) Hepatitis and AIDS Dept., Pasteur Institute of Iran, Tehran, Iran 2) Clinical Research Dept., Pasteur Institute of Iran, Tehran, Iran 3) Pediatric Infectious Disease Research Center, Tehran University of Medical Sciences, Tehran, Iran 4) Center for Communicable Disease Control, Ministry of Health and Medical Education, Tehran, Iran 5) Pediatrics Center of Excellence, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran 6) Iranian society for support of patients with infectious Disease, Tehran, Iran

Background: A nationwide HBV vaccination for neonates in the Expanded Program on Immunization (EPI) was launched in Iran in 1993. After HBV vaccines were included in the EPI, HBsAg-positive rate and anti-HBc dropped remarkably according to recent studies from different provinces of Iran. Despite the achievement of the HBV vaccination program, breakthrough infections happen uncommonly in vaccinees. Concern about the long-term success of this program still remains, because breakthrough infections due to emergence of surface mutants have been reported in immunized infant and children from different geographic areas. On the other hand occult HBV infection also has raised some concern. We therefore, aimed to evaluate the seroprevalence of HBV and vaccine escape mutants among individuals born after the initiation of the nationwide vaccination program in Iran. **Material/Methods:** A total of 1115 apparently healthy participants younger than 23 years old with approximately 223 of them in each age cohort were enrolled in the study. Presence of HBsAg, anti-HBs and anti-HBc were evaluated by ELISA kit. HBV DNA levels were measured in anti-HBc and /or HBsAg positive subjects. PCR products were sequenced directly and mutations were determined.

Results: Cases categorized in 5 age subgroups including 1-5, 6-10, 11-14, 15-18 and 19-22 years. The overall HBsAg prevalence among the 1115 cases was 0.27%. Anti-HBs, and anti-HBc positive rates were 48% (535 cases) and 0.18% (2 subjects) respectively. Out of 2 anti-HBc positive individuals, in one case, coexistence of HBsAg and anti-HBc was found (probably showing an acute infection) and the other one revealed isolated anti-HBc. HBV DNA was detected in 3 out of 4 anti-HBc and/or HBsAg positive subjects but not in patient with isolated anti-HBc. I195M within the S gene was detected in two of three HBV DNA cases. A significant trend of decrease in anti-HBs positivity was observed from ages <5 years (73.9%) to 6-10 years (49.4%), 11 to 14 years (39.7%), 15 to 18 years (33.7%), and 19 to 22 years (40.2%) (P=0.000). Position of amino acid substitutions in our positive samples is shown in fig 1.

Conclusion: A very low prevalence of HBsAg and isolated anti-HBc and no evidence of occult HBV infection reported in this cohort of study. Moreover, we revealed that mass immunization reduced HBsAg carriage and infection rates in children and adolescents than previous surveys. The mutation I195M found in the surface protein has been reported as a change produced by immune pressure. Although the number of "vaccine escape" mutants in this cohort of study is low but ongoing surveillance of breakthrough infections and close monitoring of "vaccine escape" mutants is still needed.

Fig 1: Position of amino acid substitutions in HBV isolates. The sequences determined in this study are indicated as IR111, IR222 and IR333. Mutation of I195M found in IR111 and IR333 isolates.

