Hepatitis B Serology Profiles on Children Aged 1–13 Years Old in Sumenep, Madura

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Research Report

HEPATITIS B SEROLOGY PROFILES ON CHILDREN AGED 1–13 YEARS OLD IN SUMENEP, MADURA

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ABSTRACT

Background: Hepatitis B virus (HBV) which was acquired during perinatal or childhood would promote hepatocellular carcinoma with even higher percentage than that which was acquired during adult age. That is why HBV represents a serious public health threat for children. HBV vaccination has been integrated into national expanded programme on immunization (EPI) since 1997. The aim of they study is to investigate the prevalence of HBV among children who were born after 1997 in Sumenep. Material and Methods: a total of 102 children who were born after 1997 were enrolled in this study. All children were admitted in the Emergency Room and Pediatric Ward of dr. H. Moh Anwar General Hospital for some reasons. Written informed consents were obtained from parents/ guardians of all the children. Study protocol was reviewed and approved by the Ethics Committees. All of these cases were examined for hepatitis B surface antigen (HBsAg), antibody to HBsAg (Anti-HBs), and antibody to hepatitis B core antigen (Anti-HBc). Result and Discussion: Overall, 6 (5.88%) of 102 samples were positive for HBsAg, 51 (50.00%) of 102 samples were positive for anti-HBs, and 49 (48.04%) of 102 samples were positive for anti-HBc. All the children were born after 1997. Conclusion: HBsAg rate is still high even after universal vaccination program, acquired protective antibodies against hepatitis B surface antigen were sufficient, but there is a suspicion for occult hepatitis B infections (OBI). A further study to confirm OBI is needed.

Keywords: *HBV, HBsAg, Anti-HBs, Anti-HBc, immunization*

ABSTRAK

Latar Belakang: *Hepatitis B Virus (HBV) yang diperoleh selama perinatal atau masa kanak-kanak akan menyebabkan karsinoma hepatoseluler dengan persentase lebih tinggi daripada apa yang telah diperoleh selama usia dewasa. Itulah sebabnya HBV merupakan ancaman kesehatan masyarakat yang serius bagi anak-anak. HBV vaksinasi telah diintegrasikan ke dalam program imunisasi nasional yang telah diperluas sejak tahun 1997.* ***Tujuan:*** *untuk menyelidiki prevalensi HBV antara anak-anak yang lahir setelah tahun 1997 di Sumenep. Bahan dan Metode: total 102 anak yang lahir setelah tahun 1997 yang terdaftar dalam penelitian ini. Semua anak-anak dirawat di ruang gawat darurat dan Departemenen Anak dari RSUD dr. H. Moh Anwar untuk beberapa alasan. Informed consent tertulis diperoleh dari orang tua/wali dari semua anak. Studi protokol ditinjau dan disetujui oleh Komite Etika. Semua kasus ini diperiksa untuk antigen permukaan hepatitis B (HBsAg), antibodi terhadap HBsAg (anti-HBs), dan antibodi terhadap antigen inti hepatitis B (Anti-HBc).* ***Hasil:*** *Secara keseluruhan, 6 (5,88%) dari 102 sampel yang positif untuk HBsAg, 51 (50,00%) dari 102 sampel yang positif untuk anti-HBs, dan 49 (48.04%) dari 102 sampel yang positif untuk anti-HBc. Semua anak lahir setelah 1997.* ***Kesimpulan:*** *Tingkat HBsAg masih tinggi bahkan setelah program vaksinasi universal, diperoleh antibodi pelindung terhadap antigen permukaan hepatitis B sudah cukup, tapi ada kecurigaan untuk okultisme infeksi hepatitis B (OBI). Sebuah studi lebih lanjut untuk mengkonfirmasi OBI diperlukan.*

Kata kunci: *HBV, HBsAg, Anti-HBs, Anti-HBc, imunisasi.*

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INTRODUCTION

Hepatitis B is an infectious disease caused by hepatitis B virus (HBV) that affects more than 400 million people worldwide, and 1.3 million die of decompensated cirrhosis and/or hepatocellular carcinoma (HCC) annually.[1] HBV variants are currently classified into the human genotypes A to H.[2]

Up to 90% of infected newborns develop chronic HBV infection, which gives a higher risk of HCC later in their adulthood, while 24% of adults chronically infected during childhood had either HCC or cirrhosis.[2]

A safe and effective vaccine against hepatitis B has been available since 1982. The introduction of a childhood immunization program in many countries has dramatically reduced the carrier rate of HBV and significantly decreased the incidence of HCC. In Indonesia, HBV vaccination had been introduced since 1987, and has been integrated into national expanded programme on immunization (EPI) since 1997. WHO recommends HBV vaccination to all infants, first at birth, then followed by two subsequent vaccinations with each minimum interval of 1 and 2 months respectively.[1]

However, the current serologic status of HBV in children has not been fully investigated in Indonesia. The aim of this study was to investigate the prevalence of HBV among the children who were born after the national immunization program in Sumenep, an area in East Java, Indonesia, which was with medium-to-high endemicity for HBV.

MATERIALS AND METHODS

Study subjects

Three ml of blood samples were taken from all the patients aged 1–13 who admitted in the Emergency Room (*IGD*) and Pediatric Ward (*Zaal Anak*) of dr. H. Moh Anwar General Hospital for some reasons. A hundred and two samples were collected in this study. Serum samples were obtained during January-March 2012 and were stored at -20° C until further usage. Written informed consents were obtained from parents/guardians of all the children. No individual hepatitis B vaccination records remained. The study protocol was reviewed and approved by the Ethics Committees of dr. H. Moh. Anwar General Hospital.

Serological markers of HBV infection

All refrigerated samples were tested for HBsAg with enzyme-linked immunosorbent assay (ELISA) (Hepalisa HBsAg) and for anti-HBs by enzyme-linked immunosorbent assay (ELISA) (Zhongsan Anti-HBS ELISA). In order to differentiate vaccine-induced antibody from naturally acquired antibody (and to identify the suspects of occult HBV infections), the prevalence of antibody to hepatitis B core antigen (anti-HBc) was assessed by enzyme-linked immunosorbent assay (ELISA) (Hepalisa Anti HBc).

RESULTS AND DISCUSSION

A total of 102 children were screened for serological markers of HBV infection. Overall, positivity rates for HBsAg and anti-HBs were 5.88% (6 out of 102) and 50.00% (51 out of 102), respectively, with the mean age of 5.76 years old. All the children (1–13 y.o.) were born after the introduction of the universal vaccination program. Anti-HBc rates were 48.04% (49 out of 102). Of 51 anti-HBs positive children, 23 were negative for anti-HBc. All six HBsAg-positive children were negative for anti-HBs.

Similar study in Borno State, Nigeria showed that overall seroprevalence of HBsAg among primary school pupils was 44.7%,[3] while in those 439 children in Moldova (mean age, 5 years), the prevalence of HBsAg and Anti-HBc were 6.8% and 17.1%, respectively.[4]

Successful vaccination programs had been shown by several countries which previously belonged to high prevalence HBV countries, such as in a study in Karachi, Pakistan, among sixty five (1.8%) out of 3533 children (mean age 10±4 years old) were positive for HBsAg.[5] In Taiwan, after 25 years of nationwide HBV universal vaccination program for infants, HBsAg sero-prevalence sharply declined from 9.8% to 0.6% with HBV vaccination coverage as high as 97%.[6]

This study was unable to assess the actual coverage rate because no individual vaccination records remained. For this reason, efficacy of vaccination was not evaluated in this study. However, this study did show that acquired protective antibody against HBV infection was sufficient among children born after the universal vaccination program.

The HBsAg prevalence of 5.88% in this study was still considered high. A high coverage rate for HBV vacination is crucial for decreasing the prevalence of HBV infection. Program for Appropriate Technology in Health, a non governmental organization in United States of America, (PATH) stated that Birth dose within seven days of birth was 65%, even though HBV 3 coverage was 80-85%.[7] Some of the first dose of HB vacccine in Indonesia has been administered along with the first dose of DPT, which was generally 6 weeks to 2 months of age. Delay in giving the first dose of HB vaccine would not prevent perinatal transmission.[8]

PATH worked with the Indonesian Ministry of Health since the beginning of 1987 to launch a model immunization program on the island of Lombok. The innovative program introduced a comprehensive system for delivering a vital birth dose of the vaccine and established a system for tracking and monitoring pregnancies and births. On October 2002, the Government began an effort to ensure that every newborn is administered Hepatitis B vaccines with prefilled, single use syringe and needle (Uniject®) during the first seven days of life.[7] HBsAg rates on children who were born before 2002 and after 2002 were 0% (0 out of 17) and 7.05% (6 out of 83) respectively. This concludes that even after PATH Uniject® programs in 2002, there had not been any effect in Sumenep.

On the other hand, there was 0% HBsAg rate in children aged 10–13 y.o., means before PATH Uniject® program was promoted? while it was 7.05% in those born after. Anti-HBc rate in previous groups was as high as 47.06%. This means that they had ever been infected before.

Our study showed that HBsAg rate in children Sumenep was still considered high. Hepatitis B immunization coverage of 18.1% in Sumenep, data from National Basic References of Ministry of Health 2007, could be one of the factors which supported this fact.[9] PATH's Uniject® program was one of the solutions to increase the Hepatitis B immunization coverage of birth dose, but it had no significant impact in our study in Sumenep. Some other factors which might have played a role in this result should be searched and overcomed.

The ACIP, the American College of Obstetrics and Gynecology (ACOG), the American Academy of Family Practice (AAFP), and the American Academy of Pediatrics (AAP) recommend that all pregnant women receive prenatal testing for hepatitis B during each pregnancy by screening serum for the presence of HBsAg, regardless of risk factors or immunization history.[10] This routine HBV serological profile screening on pregnant women should be the target of the Ministry of Health of Indonesia in the near future. On pregnant women with positive HBsAg, HBV vaccination and HBIg (0.5 ml) should be administered on their babies within 12 hours after birth.[11] These efforts will lead to a greater control of HBV infection, and furthermore, liver diseases caused by HBV infection would be better controlled.[12] The remaining challenges will be to minimize the rate of vaccine failure and to deal with potential vaccine-related events, such as the emergence of escape surface mutants.[13]

Further studies with larger samples in the future will accomodate better reflections of HBV immunology profile in children. HBV DNA detection among those with HBsAg negative, anti HBc positive, and or anti HBs positive or negative should be tested in order to detect occult HBV infections.

In conclusion, HBsAg rate among children born after the Hepatitis B universal vaccination program is still high in Sumenep, acquired protective antibodies against HBV infection were sufficient, and suspects of occult hepatitis B infections were found. Continuation in PATH's Uniject® program, implementation of immunization programs, and routine HBV serological profile screening on pregnant women should proceed to eradicate HBV infection. Some other aspects which play roles in the high HBsAg rates should be explored, including molecular studies.

Table 1. Seroprevalence of hepatitis B surface antigen (HBsAg), anti-HBs, and anti-HBc among study population

	No.	No. Positive	%
HBsAg	102	6	5.88
Anti-HBs	102	51	50.00
Anti-HBc	102	49	48.04

Table 2. Comparison of prevalence of hepatitis B markers in children born before and after PATH's Uniject® programs.

Age	HBsAg			Anti-HBs			Anti-HBc		
(Years)	No.	Pos.	%	No.	Pos.	%	No.	Pos.	%
1–9	85	6	7.05	85	41	48.23	85	41	48.23
10–13	17	0	0	17	10	58.82	17	8	47.06

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REFERENCES

1. Wittet S (2001). Hepatitis B Vaccine Introduction: Lessons Learned in Advocacy, Communication, and Training. Children's Vaccine Program; 1–3.
2. Simmonds P, Midgley S (2005). Recombinant in the genesis and evolution of hepatitis B virus genotypes. Journal of Virology; 79: 467–76.
3. Bukbuk D, Bassi A (2005). Sero-prevalence of hepatitis B surface antigen among primary school pupils in rural Hawal valley, Borno State, Nigeria. Journal of Community Medicine and Primary Health Care. June; 17(1): 20–3.
4. Drobeniuc J, Hutin Y (1999). Prevalence of Hepatitis B, D, and C virus infections among children and pregnant women in Moldova: additional evidence supporting the need for routine hepatitis B vaccination of infants. Epidemiology of Infectious Disease June; 123(3): 463–7.
5. Jafri W, Yakoob J (2006). Hepatitis B and C: prevalence and risk factors associated with seropositivity among children in Karachi, Pakistan. BMC Infectious Disease; 6: 101.
6. Hsuan N (2009). HBV Now in Asia. Hepatitis B Vaccination in Children. Japan Society of Hepatology. Japan; 42.
7. Nelson C, Widjaya A (2002). Using Uniject™ to Increase the Safety and Effectiveness of Hepatitis B Immunization. Program for Appropriate Technology in Health (PATH) and PATH's Children's Vaccine Program; 1–8.
8. Levin C, Moniaga V (2005). The cost of home delivery of a birth Dose of Hepatitis B Vaccine in a prefilled syringe in Indonesia. Bulletin of the World Health Organization June, 83(6); 456–61.
9. Soendoro T (2007). Laporan Riset Kesehatan Dasar Tahun 2007 Provinsi Jawa Timur. Badan Penelitian dan Pengembangan Kesehatan Departemen Kesehatan RI Jakarta; 61–6.
10. Mast EE, Margolis HS, Fiore AE, et al (2005). A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization

of infants, children, and adolescents. MMWR. 2005; 54(RR-16): 1–31.
11. Ranuh I, Suyitno H (2011). Pedoman Imunisasi di Indonesia. Hepatitis B; VIII.1; 256–63.
12. Chang MH, Chen CJ, et al. 1997. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. New England Journal of Medicine; 336: 1855–9.
13. Hsu Y, Chang H, et al. 1999. Changes of hepatitis B surface antigen variants in carrier children before and after universal vaccination in Taiwan. Hepatology; 30: 1312–7.

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