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Original Article

Hepatitis B serologic patterns in children of HBV carriers or infected mothers

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ABSTRACT

Background Vertical transmission is usually the cause of increasing carrier rates for hepatitis B infection, especially in highly endemic areas.

Objective To determine the serologic patterns of hepatitis B in children of HBV carrier/infected mothers.

Methods This was a cross sectional study on children of HBV carrier/infected mothers. Subjects were recruited consecutively and examined at the Department of Child Health, Cipto Mangunkusumo Hospital during January–July 2003. Children were included if they were generally healthy and their parents gave permission. Children with chronic illness, previous blood transfusions, or drug abuse were excluded.

Results Fifty-nine children of 32 HBV carrier/infected mothers were recruited. HBsAg was positive in 8 children, anti-HBs in 37, and anti-HBc in 4 children. Seventy-three percent of children had been vaccinated against HBV but only 81% had positive anti-HBs. Of eighteen children who received hepatitis B vaccine and HBIg at birth, none was infected. Six out of 25 children who received only hepatitis B vaccine were infected.

Conclusion HBsAg, anti-HBs, and anti-HBc were positive in 14%, 36%, and 7% of children of HBV carrier/infected mothers, respectively **[Paediatr Indones 2004;44:176-180].**

Keywords: *hepatitis B, immunization, perinatal transmission*

Hepatitis B remains a globally important disease. There are approximately 350 million hepatitis B virus (HBV) carriers in the world, and perhaps 1-2 million die every year from cirrhosis and/or hepatocellular carcinoma (HCC). Perinatal or vertical transmission is one of the most efficient modes of spreading HBV which results in increasing carrier rates, especially in highly endemic areas.[1-3]

The disease is endemic in several regions such as Indonesia, with a carrier rate of 5-10% in the general population. Approximately 90% of infants of infected mothers become carriers.[4-6] The management of hepatitis B, especially in children, is still a problem since there is no effective therapeutic drug. Therefore, in areas with high endemism, WHO recommends immunization to break the chain of infection, reduce the pool of virus carriers, and ultimately reduce the burden of serious liver disease.[7-10] Universal vaccination in neonates is an imperative strategy to prevent perinatal transmission, thus reduce the pool of chronic carriers.[9-10] In Indonesia, a hepatitis B mass immunization program began in April 1997.[11]

The aim of this study was to determine the serologic patterns of hepatitis B in infants and children of HBV carrier/infected mothers at Cipto Mangunkusumo Hospital, Jakarta.

Methods

This was a cross-sectional descriptive study on children of HBV carrier/infected mothers who came to the Hepatology Outpatient Clinic of the Department of

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Internal Medicine, Cipto Mangunkusumo Hospital, Jakarta, during 2002. Children were consecutively recruited in January-July 2003 and then examined in the Outpatient Clinic, Department of Child Health of the same hospital. Children were included if they were healthy and their parents agreed to participate in the study. Exclusion criteria were chronic diseases, previous blood transfusion, and drug abuse. History, physical examination, and blood samples for HBsAg, anti-HBs, and anti-HBc titers determination using ELISA method were taken. Data were processed using SPSS 11.0 computer program.

Results

In the period of January-July 2003, 59 children from 32 HBV carrier/infected mothers consisting of 31 boys and 28 girls participated in the study. Eighteen (30%) were under the age of 5. The subjects' characteristics are shown in **Table 1.**

TABLE 1. SUBJECTS' CHARACTERISTICS

Children (n = 59)		**Mothers (n= 32)**	
Age (year)		**Age (year)**	
≤5	18	≤30	5
>5	41	>30	27
Average (SD)	8.91 ± 5.3	Average (SD)	36.31 ± 5.6
Range	0.75-17.0	Range	27.0 – 47.0
Sex		**Education**	
Male	31	Low	10
Female	28	Moderate	20
History of birth		High	2
Spontaneous labor	48	**Occupation**	
Cesarean section	11	Housewife	6
HBV immunization status		Working	26
Active	25	**Number of children**	
Active + Passive	18	≤2	20
No immunization	16	>2	12

TABLE 2. SEROLOGICAL PATTERNS OF HBV INFECTION

Serologic	**Male (n = 31)**	**Female (n = 28)**	**Total**
HbsAg			
Positive	3	5	8
Negative	28	23	51
Anti-HBs			
Positive	18	19	37
Negative	13	9	22
Anti-HBc			
Positive	3	1	4
Negative	28	27	55

Table 2 shows serological patterns of HBV infection. Positive HBsAg was found in 8 (14%) subjects (3 boys and 5 girls), anti-HBs in 37 (63%) subjects consisting of 18 boys and 19 girls, and anti-HBc in 4 (7%) subjects (3 boys and 1 girl).

Most of the children (43 of 59) had been immunized against HBV and 35 of them had positive immune response. Eighteen of the 43 immunized children received hepatitis B vaccine and hepatitis B immune globulin (HBIg), while 25 children received only hepatitis B vaccine. None of the children who received vaccine and HBIg was infected, but 6 children who received only active vaccination were infected. **Table 3** shows immunization status, serologic status, and timing of the first HBV immunization.

TABLE 3. IMMUNIZATION STATUS, SEROLOGIC STATUS, AND TIME OF THE 1ST IMMUNIZATION

	Serological status*					Total
	Infected			Not Infected		
	+/+/+	+/-/+	+/-/-	-/+/-	-/-/-	
No Immunization	0	0	2	0	14	**16**
Active immunization						
≤ 12 hours	0	0	0	1	0	**1**
> 12–24 hours	0	0	0	1	0	**1**
> 24 hour – 7 days	0	0	0	1	0	**1**
> 7 days	2	2	2	14	2	**22**
Active and Passive immunization						
≤12 hours	0	0	0	16	0	**16**
> 12–24 hours	0	0	0	2	0	**2**
> 24 hour–7 days	0	0	0	0	0	**0**
> 7 days	0	0	0	0	0	**0**
Total	**2**	**2**	**4**	**35**	**16**	**59**

*HBsAg/anti-HBs/anti-HBc

Among the eight children with positive HBsAg, four were born to carrier mothers who had no data regarding their HBeAg and anti HBeAg status, and two were born to infected mothers with negative HBeAg and anti-HBe; one from a carrier mother with positive HBeAg and negative anti-HBe, and one from a carrier mother with negative HBeAg, positive anti-HBe, and positive DNA-VHB. The relation between serological status of the children and their mothers are listed in **Table 4.**

TABLE 4. THE RELATION OF SEROLOGICAL STATUS BETWEEN MOTHERS AND THEIR CHILDREN

Mother's serological status	Children's serological status*						
	Infected				Not Infected		
	+/+/+	+/-/+	+/-/-	Total	-/+/-	-/-/-	Total
HbsAg	2	0	2	4	25	12	37
HBsAg (+)/HBeAg (-)/Anti-HBe (-)	0	2	0	2	8	4	12
HBsAg (+)/HBeAg (+)/Anti-HBe (-)	0	0	1	1	2	0	2
HBsAg (+)/HBeAg (-)/ Anti-HBe (+)/DNA-HVB (+)	0	0	1	1	0	0	0

*HBsAg/anti-HBs/anti-HBc

Discussion

The epidemiology of HBV infection in women of childbearing-age and their children has an important implication on strategies for prevention and control of the disease.[1-3] In this study we found that 8/59 (14%) children showed positive HBsAg, 37/59 (63%) showed positive anti-HBs, and 4/59 (7%) showed positive anti-HBc. The prevalence of HBsAg is quite similar to the result of a study by Widjaja in an orphanage,[12] where prevalence of HBsAg was 12%. This was higher than the prevalence in the general population as reported by Akbar (4.1%)[4] and in pregnant women as reported by Wiharta (5.2%).[13]

The youngest patient in this study was 9 months old and the eldest was 17 years old (mean 8.91, SD 5.3 years). Eight children were infected, 7 of them were older than 5 years. Age is important, because the higher the age, the higher the risk of contact with a HBV positive person is, if they have never been immunized.[5-6]

The eight infected children showed different serological profiles. Positive HBsAg, negative anti-HBs and anti-HBc were seen in four children. Two showed positive HBsAg and anti-HBc, and negative anti-HBc. The other two showed positive HBsAg, anti-HBs, and anti-HBc, which were thought to be due to mutation. Mutation involving 2 brothers from an infected mother was reported by Ho in Taiwan. The two children had been immunized, but serology showed that they were infected even though they had anti-HBs with a protective level (>10 mIU/mL).[14] Mutation happened as the result of viral defense mechanism against active or passive prophylaxis immunization.[15] The prevalence of mutation in Indonesia is still unknown; but in Taiwan it is around 22.7% and in Singapore 42%.[14-16]

Forty-three out of 59 children had already been immunized against HBV, but only 35 were immune. Two children had negative anti-HBs even though they were not HBV infected. We assumed that anti-HBS was not detected because the level of anti-HBS had already decreased. It is known that the antibody after immunization will decrease with time, but immune memory will be present up to 13 years after the immunization, so children and adults with undetectable anti-HBs will still be protected from HBV infection.[10,16-19] In this study, 18 children who had received both active and passive immunization at the age of less than 7 days were not infected by HBV. Six out of 25 children who only received active immunization at the age of more than 7 days were infected. The efficacy of prophylactic HBV immunization with or without HBIg had been evaluated in a longitudinal study.[17-19] Beasley reported that 80-95% of babies from positive HBsAg mothers who received HBV immunization and HBIg prophylaxis soon after birth were not infected by HBV.[19] Zamir reported that 89% of babies from negative HBeAg carrier mothers who only received active immunization soon after birth developed protective levels of anti-HBs.[20]

This study also showed that immunization coverage was high in children under five, 17/18 (94%) compared to 26/41 (64%) in children over 5 years. This may be due to mass HBV immunization in Indonesia which started in April 1997. Before that, the price of the vaccine was relatively expensive and unaffordable to many people.[5,6,11]

Fourteen children were not infected even though they were not immunized, which may have something to do with their mother's serological status. According to the literature, mother's serological status has an important role in vertical transmission.[1-3,7,21] Children born to positive HBeAg carrier mother has 70-90% chance to be infected, [2-3] while if only HBsAg is

detected, the chance is around 22-67%.[2] Carrier mothers with positive anti- HBe have the lowest capacity for vertical transmission, but their infants can develop fulminant hepatitis.[22] It is a pity that in this study only 12 out of 32 mothers were tested for other serological markers. From 9 mothers with negative HBeAg and anti HBe, 2 children were infected, while 2 children of two mothers with positive HBeAg and negative anti HBe were infected. One mother with negative HBeAg, positive anti HBe, and positive HBV-DNA, had one infected child.

It is unkown whether transmission of HBV in this study was vertical or horizontal. In Indonesia and other Asian countries, both modes (vertical and horizontal transmission) are common. Soewignyo reported that in Mataram, Lombok, the rateof horizontal transmission is higher.[5-6] The same result was also reported by Widjaja in a study at an orphanage in Jakarta.[12] This condition was due to close contact with a HBV infected person. Besides close contact, equipment sharing and the length of stay in the orphanage also influenced the rate of infection. Frank reported that 15 out of 226 (6.6%) South East Asian children born to healthy mothers in the United States were infected by HBV.[23]

In conclusion, HBsAg, anti-HBs, and anti-HBc were positive in 14%, 36%, and 7% of children of HBV carrier/infected mothers, respectively.

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