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Epidemiological survey of hepatitis B virus infection in Chiang Mai, 1981~1982

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Summary

Fifty-nine school children at Wat Kau Khum (WKK) School, Chiang Mai Province, and 52 children and their parents under the care of the Comprehensive Child Care Clinic (CCCC), Chiang Mai University were tested for HBsAg and anti-HBc in their blood. Eighteen HBsAg-positive specimens were tested also for HBeAg and anti-HBe. Determinations of the HBV-serological markers were done by using the enzyme-linked immunosorbent assay (ELISA). HBsAg was found in 27.0% (17/63) of the children at WKK, in 7.6% (4/53) of the children and 5.4% (3/56) of the parents at CCCC. Twenty percent (3/15) of HBsAg-positive children at WKK were HBeAg-positive. Anti-HBc was positive in 45.0% of the children at WKK and in 47.3 to 52.0% of the children and parents at CCCC, but percentages of anti-HBc positive were estimated at 86.7% for WKK and 84.6 to 93.9% for CCCC, if border-line values were referred to as positive. This means more than 50% of the study subjects had a history of HBV infection. Study on paired sera from children and parents at CCCC revealed that 92.0% (46/50) of the children from HBsAg-negative parents were free from the antigen, and 68.0% (17/25) of the children from anti-HBc-positive parents were positive for the antibody, whereas only 20.0% (1/5) of the children from anti-HBc-negative parents had the antibody.

Key words : hepatitis B virus, Chiang Mai, epidemiology

Introduction

Hepatitis B infection is a major health problem in many countries, especially in Asia and tropical Africa¹⁾ and in limited areas even in developed countries where the infection appears to be endemic²⁾. Hepatitis B virus (HBV) infections can be classified into four categories i.e. subclinical infection, acute hepatitis, fulminant hepatitis and chronic hepatitis³⁾. Chronic carriers of HBV run a high risk of developing chronic liver diseases including hepatic failure, cirrhosis and primary hepatocellular carcinoma^{4~6)}. Chronic carriers

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of HBV represent a sole reservoir of the virus, since their blood, blood products and other body fluids contain the virus which is transmitted to healthy persons mainly via parenteral routes as well as via close direct contact including perinatal vertical infection^{7,9)}.

The association of hepatitis B surface antigen (HBsAg) with viral hepatitis B has been confirmed, as it appeared in the blood of patients suffering from acute hepatitis. In asymptomatic carriers, HBsAg persists for months and probably for years^{9,10)}. The e-antigen (HBeAg) and its antibody (anti-HBe) have been found to construct an antigen-antibody system associated with the hepatitis B virus infection^{11,12)}. It has been suggested that HBeAg is associated with the development of chronic hepatitis in HBsAg carriers while the presence of anti-HBe is not associated with chronic hepatitis¹²⁻¹⁵⁾. The concept that the presence of HBeAg in blood is a marker of the infectivity of the patient is supported by its association with the presence of hepatitis B core antigen (HBcAg) in the nuclei of hepatocytes¹⁶⁾, and of HBV-specific DNA polymerase as well as of Dane particle in the serum¹⁷⁾. The other serological marker, anti-HBc was found to be associated either with the asymptomatic carrier state or noncarrier state of HBsAg¹⁸⁾.

Infections with HBV are common among Thai people. The prevalence of HBsAg in the general population in Bangkok was 9~10% during the period 1973~1975^{19,20)}. In Chiang Mai, HBsAg was found in 10% of the general population in 1973¹⁹⁾. Our previous study in 1981~1982 showed that 40.0% of the general population aged between 16 and 80 years had been infected with HBV, i.e. 16.7% were positive for HBsAg and 23.7% were positive for anti-HBs²¹⁾. However, there is no report available describing the distribution of HBsAg in children in Chiang Mai. It is the purpose of this epidemiological study to determine the incidence of HBV serological markers among children of low socioeconomic status in a rural area and among families under a developed health care system.

Materials and Methods

The subjects in this study were 63 children, 9 to 14 years of age, attending Wat Kau Khum (WKK) school near Chiang Mai, and 53 children, 7 to 15 years of age, who were under the care of the Comprehensive Child Care Clinic (CCCC), Chiang Mai University and their 56 parents. The serum samples were collected from WKK in August, 1981 and from CCCC in August, 1982.

The serum samples were tested for HBsAg, HBeAg, anti-HBe and anti-HBc with the enzyme immunoassay by using AuszymeTM, HBe-ETA and CorzymeTM, respectively, purchased from Abbott Laboratories (North Chicago, Ill.). Tests of HBeAg and anti-HBe were applied only for sera in which HBsAg were found with AuszymeTM.

Results

1. *Comparison between children at Wat Kau Khum (WKK) and children at the Comprehensive Child Care Clinic (CCCC)*

The prevalence of HBV serological markers among children at WKK school, children and their parents at CCCC is presented in **Tables 1 and 2**. The children at

WKK had a higher incidence of HBsAg (17/63, 26.98%), than the children at CCCC (4/53, 7.54%) ($p < 0.01$).

HBsAg-positive children of both groups (WKK and CCCC) were tested for HBeAg and anti-HBe (Table 2). At WKK, 20.0% (3/15) and 29.41% (5/19) of the children were positive for HBeAg and anti-HBe, respectively, if anti-HBe $\pm$ was referred to as positive, while 46.67% (7/15) were negative for both the antigen and the antibody. At CCCC, 75.0% (3/4) and 25.0% (1/4) were positive for HBeAg and anti-HBe, respectively, if anti-HBe $\pm$ was referred to as positive. The percentage of HBeAg-positive was higher at

Table 1 Incidence of HBV serological markers among children at WKK, and children and their parents at CCCC in Chiang Mai Province (1)

Status for HBV serological markers	CCCC		WKK
	Parents	Children	Children
HBsAg (+), HBeAg (+), anti-HBe (-), anti-HBc (+)	1	2	3
HBsAg (+), HBeAg (+), anti-HBe (-), anti-HBc (+)	0	0	0
HBsAg (+), HBeAg (-), anti-HBe (+), anti-HBc (+)	0	1	2
HBsAg (+), HBeAg (-), anti-HBe ($\pm$), anti-HBc ($\pm$)	0	0	2
HBsAg (+), HBeAg (-), anti-HBe (-), anti-HBc (+)	0	0	2
HBsAg (+), HBeAg (-), anti-HBe (-), anti-HBc ($\pm$)	1	0	4
HBsAg (-), anti-HBc (+)	25	24	19
HBsAg (-), anti-HBc ($\pm$)	23	17	19
HBsAg (-), anti-HBc (-)	5	8	8
Number of tested serum samples	55	52	59

Table 2 Incidence of HBV serological markers among children at WKK, children and their parents at CCCC in Chiang Mai Province (2)

HBV markers	CCCC		WKK
	Parents	Children Age, 7~15 yrs (9.1 $\pm$ 1.6**)	Children Age, 9~14 yrs (11.4 $\pm$ 1.2)
HBsAg +	3/56* (5.35)	4/53 (7.54)	17/63 (26.98)
HBsAg +			
HBeAg +, anti-HBe -	1/3 (33.33)	3/4 (75.0)	3/15 (20.0)
HBeAg -, anti-HBe +	1/3 (33.33)	1/4 (25.0)	2/17 (11.76)
HBeAg -, anti-HBe $\pm$	0/3 (0)	0/4 (0)	3/17 (17.65)
HBeAg -, anti-HBe -	1/3 (33.33)	0/4 (0)	7/15 (46.67)
HBsAg +			
anti-HBc +	1/2 (50.0)	3/3 (100)	8/14 (57.14)
anti-HBc $\pm$	1/2 (50.0)	0/3 (0)	6/14 (42.86)
anti-HBc -	0/2 (0)	0/3 (0)	0/14 (0)
HBsAg -			
anti-HBc +	25/53 (47.17)	24/49 (48.98)	19/46 (41.30)
anti-HBc $\pm$	23/53 (43.40)	17/49 (34.69)	19/46 (41.30)
anti-HBc -	5/53 (9.43)	8/49 (16.33)	8/46 (17.39)
+	26/55 (47.27)	27/52 (51.92)	27/60 (45.0)
anti-HBc $\pm$	24/55 (43.64)	17/52 (32.69)	25/60 (41.67)
-	5/55 (9.09)	8/52 (15.38)	8/60 (13.33)

* Denominators are number of serum samples. ** Mean $\pm$ SD.

Figures in parenthesis are percentages.

CCCC than at WKK in the *chy* square test ($\chi_s^2=4.42$, $p<0.05$), but the difference was not significant when the Yates' modification was applied to the test ($\chi_s^2=2.24$, $p>0.1$). A significant difference of the distribution of anti-HBc was not found between the two groups, and about 80% of each group had the antibody, if $\pm$ was referred to as positive (Table 1, 2).

2. Comparison between children and their parents at CCCC

Table 3 describes the prevalence of HBsAg among children at CCCC in relation to their parents. Three parents who possessed HBsAg had HBsAg-negative children. Only four children of the 53 parents, who were HBsAg-negative, had HBsAg in the sera. The percentage of HBeAg-positive appeared to be higher in the children than the parents, but a final conclusion could not be drawn because the number of specimens was small (Table 2).

All of the HBsAg-positive persons at CCCC had anti-HBc but 41 out of 49 HBsAg-negative children (83.7%) and 48 out of 53 HBsAg-negative parents (90.6%) also had anti-HBc, if $\pm$ was referred to as positive (Table 2). Table 4 shows the correlation of anti-HBc between children and their parents at CCCC. Seventeen children from 26 anti-HBc-positive parents (65.4%) were positive for the antibody, and two children from five anti-HBc-negative parents (40%) were negative for the antibody. Three children from 26 anti-HBc-positive parents (11.5%) were antibody-negative, and one child from five antibody-negative parents (20%) was antibody-positive.

Discussion

Children at WKK had a higher incidence of HBsAg compared to those at CCCC, $p<0.01$ (Table 1, 2). However, anti-HBc was detected at almost equal frequencies in both groups. These results indicate that the HBV infection

Table 3 The incidence of HBsAg among children at Comprehensive Child Care Clinic in relation to their parents

	Children		Total number
	HBsAg(+)	HBsAg(-)	
Parents*			
HBsAg +	0	3	3
HBsAg -	4	46+3*	53
Total number	4	49	53

* For three children, both parents were tested.

Table 4 The incidence of anti-HBc among children at Comprehensive Child Care Clinic in relation to their parents

	Children			Total number
	Anti-HBc(+)	Anti-HBc($\pm$)	Anti-HBc(-)	
Parents*				
Anti-HBc +	17	5+1*	3	26
Anti-HBc $\pm$	9+2*	9	3	23
Anti-HBc -	1	2	2	5
Total number	27	16	8	51**

* For three children, both parents were tested.

** One child and one parent were not tested.

occurred at equal frequencies in both groups, but the infection in WKK-children resulted in the HBsAg-carrier state more frequently than in CCCC-children. Apparently the children at WKK had been brought up under lower socioeconomic and poorer sanitary conditions than those of CCCC. The results of this experiment suggest that socioeconomic and environmental conditions may play a role in determining the outcome of HBV infection, and the vertical infection was more frequent in WKK than CCCC group.

Among the HBsAg-positive children at WKK, 20% had HBeAg, 29.41% had anti-HBe, and 46.67% were negative for both HBeAg and anti-HBe. Among the HBsAg-positive children at CCCC, 75% had HBeAg and 25% had anti-HBe. The frequency of HBeAg-positive was slightly higher in the children at CCCC than in the children at WKK. One explanation is that, among the children who possessed HBsAg at the time of collecting blood specimens, the past HBV infection of children at WKK occurred at an earlier age than those of CCCC since HBeAg persists for a shorter period than HBsAg⁹⁾.

The high anti-HBc prevalence of more than 82% among children at WKK as well as at CCCC indicated that remote past infections of HBV had occurred in the majority of these two groups.

Our study on the incidence of HBsAg among children at CCCC and their parents revealed that three parents who possessed HBsAg had children negative for HBsAg. This finding indicates that these three children might have acquired the infection from their parents but had recovered from the carrier state before the time of collecting blood, since none of the children was anti-HBc negative. Four out of 53 HBsAg-negative parents had children who were positive for HBsAg. There may be a possibility that these parents infected their children at a time when they were in a high infectivity period, since none of the parents was negative for anti-HBc. In 46 out of 53 pairs, both children and parents were negative for HBsAg. It may be assumed that some pairs have no history of HBV infection, or some of the parents transmitted the virus to their children while they were in a high infective period and then all of them subsequently became HBsAg free, but infection from outside of the family is not excluded.

A significant statistical difference between adults and children at CCCC was not found in the presence of HBeAg or of anti-HBe as far as HBsAg-positive persons were concerned, though 3/4 of the children were positive for HBeAg whereas 1/3 of the adults were positive (**Table 2**).

We also studied the prevalence of anti-HBc in parents and their children. Twenty-six parents who possessed anti-HBc had 17 children with anti-HBc + and five with anti-HBc ±. Five parents who were negative for anti-HBc had one child with anti-HBc + and two children with anti-HBc ± (**Table 4**). These results suggest that infection within a family was common in this study group.

The incidences of HBsAg in our study groups were 26.98% of children at WKK, 9.54% of children at CCCC, and 5.35% of parents at CCCC. These high incidences of HBsAg have been described elsewhere also by other investigators. Punyagupta et al.¹⁹⁾ reported in 1973 that the incidence of HBsAg among the general population of Chiang

Mai Province was 10%. Our previous study in 1981~1982 showed that 16.7% of the general population aged between 16 and 80 years were positive for HBsAg²¹⁾. In Bangkok in 1971, 10.9% of children aged between 5 and 9 years and 7.9% of children aged between 10 and 14 years were positive for HBsAg²²⁾. In 1973 Punyagupta et al.¹⁹⁾ studied children and found that in Bangkok 5.2% were positive for HBsAg whereas in the central part (Ayudhya) 14% were positive for the antigen. Beasley and coworkers²³⁾ studied Chinese preschool children and found that 7.8% were positive for HBsAg. Whittle et al.²⁴⁾ studied two Gambian villages in West Africa and found a peak of 36% in the 5~9 year-old age-group in one village and 17.6% in the 2~4 year-old age-group in another village.

In developing and tropical areas of the world, HBV infection occurred at early ages²⁵⁾, and according to the WHO Hepatitis Information 1979, the percentages of HBV carriers among the general population were 9.93% for Burma, 5.2% for Indonesia, 2.7% for Japan, 10.2% for Thailand and 6.89% for all of Asia.

The percentages of detected HBV serological markers in our study groups are considerably higher, although our results cannot always be taken to represent the real frequency of the incidence of HBV infection. The pattern of HBV serological markers in the CCCC group reveals that infection within families including maternal-infant or paternal-infant transmission may be common.

One of the most important problems regarding HBV infections is the interruption of the spread of HBV especially from mother to newborn child. This will be prevented by treatment with HB-immunoglobulin (HBIG) of infants born to HBsAg especially HBeAg positive mothers²⁶⁾, and by immunization with HBV vaccine of the infants as well as HBcAg-negative people.

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