

HEPATITIS B PROBLEM IN THAILAND

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INTRODUCTION

Hepatitis B virus (HBV) infection is one of the major communicable diseases in Thailand. Unlike hepatitis A, acute hepatitis B can progress to chronic liver disease, cirrhosis and hepatocellular carcinoma. Hepatitis including HBV infection has been part of the national surveillance system since 1971. However, the precise prevalence of hepatitis B is not known because insensitive assays are being used in some areas. Therefore, the magnitude of the problem can only be estimated by an analysis of recent epidemiologic studies. This knowledge is needed to identify population at high risk and to provide information for planning HBV control measures.

Acute Hepatitis B in Thailand

According to the national surveillance data, the case rate of acute hepatitis per 100,000 population increased from 10.58 in 1972 to 27.76 in 1979, then rapidly decreased to 17.22 in 1983. However, the actual incidence is believed to be much higher as shown by a 5 year retrospective study of 115,559 Thai military family members where an incidence of acute hepatitis B was 460-470 per 100,000 population per year (Punyagupta *et al.*, 1975). Most of the hepatitis cases reported in the national surveillance data were unspecified hepatitis and only about 0.5% were identified as hepatitis B. In contrast, hospital data revealed HBV to be the major aetiological factor in adults being responsible

for 50% to 70% of acute hepatitis cases (Burke and Snitbhan, 1980; Punyagupta *et al.*, 1973).

Prevalence of hepatitis B in Thailand

The prevalence in a community will depend on a wide range of factors, including social customs and population density. In different populations there may be striking differences in the age of acquiring the infection and in whether it is predominantly rural or urban. The identification of HBV-associated antigens, including HBsAg and its subtypes, HBeAg and HBcAg, and their respective antibodies has had a major effect on our understanding of the epidemiology of HBV infection.

Hepatitis B in the general population

In Thailand, several thorough prevalence surveys have been conducted in urban and rural populations. The methods for HBsAg detection employed by various investigators ranged from the least sensitive technique, simple immunodiffusion to very sensitive techniques such as radioimmunoassay. As shown in Table 1, reports of prevalence of HBsAg range from 5.0% to 11.8%. The prevalence of HBsAg was 5.0% to 9.0% in urban populations and 5.5% to 11.8% in rural populations. From these data, the average prevalence of HBsAg is 8.9% or approximately five million Thais are harbouring HBV and there appear to be no significant difference in prevalence between different geographical regions.

Table 1

Prevalence of HBsAg in various Thai populations.

Area	Province	Sample size	Diagnostic procedure	HBsAg(%)	Investigators (year of study)
urban	Bangkok	120	CIEP	5.0	Sangkawibha (1978)
	Bangkok	697	IEOP & RIA	8.2	Grossman <i>et al.</i> (1975)
	Bangkok	687	RIA	9.0	Scott (1973)
	Bangkok	1495	CFT & ID	9.0	Punyagupta <i>et al.</i> (1973)
	Nakhon Rachasima	219	CIEP	5.0	Sangkawibha (1978)
rural	Ayudhya	406	CFT & ID	11.8	Punyagupta <i>et al.</i> (1973)
	Cha-Cherng-Sao	120	CFT & ID	10.0	Punyagupta <i>et al.</i> (1973)
	Chantaburi	472	RPHA	10.4	Sriratanaban <i>et al.</i> (1983)
	Prachinburi	736	RIA	7.2	Scott <i>et al.</i> (1977)
	Nakhon Rachasima	484	RIA	10.1	Snitbhan <i>et al.</i> (1976a)
	Ubol	227	CFT & ID	8.4	Punyagupta <i>et al.</i> (1973)
	Lampoon	55	CIEP	5.5	Sangkawibha (1978)
	Chiengmai	116	IEOP	8.6	Snitbhan <i>et al.</i> (1975)
	Chiengmai	541	CFT & ID	10.0	Punyagupta <i>et al.</i> (1973)

CIEP = Counterimmunoelectrophoresis

ID = Immunodiffusion

IEOP = Immunoelectro osmophoresis

RTA = Radioimmuno assay

CFT = Complement fixation test

RPHA = Reverse passive hemagglutination

Age and sex distribution

From a few studies of age specific prevalence, HBsAg was found in all age groups and seemed to follow a similar pattern (Table 2). There was a low prevalence in age 0-4 years with a tendency of higher rates in older age groups. In most studies males were more frequently HBsAg positive (Snitbhan *et al.*, 1976a; Scott *et al.*, 1977; Sobeslavsky, 1980) but in a report by Grossman *et al.*, (1975) the male to female ratio was 1 to 1.4.

An evidence of exposure to HBV infection can be determined by combining the prevalence of HBsAg and anti-HBs. Approximately 10% to 20% of children under 5 years showed serologic evidence of HBV infection (Table 2). This rate rose steadily to a plateau of 40% to 60% by the age of 20 and then remained fairly constant in adult years. These four independent studies revealed a

consistent pattern of exposure and immune response to HBV infection and indicated that about half of Thai population have been exposed to HBV by the age of 20. Nevertheless, more extensive surveys are needed to define the pattern of infection in the general population.

Hepatitis B in hospital personnel

Epidemiologic data from developed countries have shown that high risk groups are those who have higher chances of exposure to infective cases or to contaminated blood and blood products. In Thailand several prevalence surveys of HBV infection have been conducted on health personnel of various hospitals. The reported prevalence of HBsAg among hospital personnel ranged from 3.6% to 11.0% (Chainuvati *et al.*, 1980; Pongpipat *et al.*, 1979; Sobeslavsky, 1980) and appeared

Table 2
Age-specific prevalence of HBV in Thai populations.

Age-group	HBsAg				HBsAg + anti-HBs			
	No. posit (%)*	No. posit (%)**	No. posit (%)***	No. posit (%)****	No. posit (%)*	No. posit (%)**	No. posit (%)***	No. posit (%)****
0 - 4	3 (4.5)	2 (4.1)	1 (1.6)	1 (1.4)	7 (21.2)	7 (14.5)	12 (19.3)	10 (13.9)
5 - 9	12 (10.9)	2 (3.2)	4 (8.1)	11 (8.6)	28 (31.5)	8 (12.9)	11 (22.4)	36 (28.1)
10 - 14	10 (7.9)	14 (14.4)	5 (19.2)	9 (6.9)	44 (42.3)	46 (47.4)	10 (38.4)	56 (43.8)
15 - 19	9 (9.7)	8 (9.5)	4 (7.8)	8 (10.9)	41 (60.3)	30 (35.7)	16 (31.4)	38 (52.0)
20 - 29	9 (8.2)	20 (10.9)	24 (12.9)	12 (9.8)	40 (62.5)	111 (61.7)	82 (44.0)	65 (52.8)
30 - 39	4 (5.0)	6 (7.3)	8 (10.6)	5 (5.9)	44 (66.7)	54 (65.8)	33 (44.0)	47 (55.3)
40 - 49	} 5 (5.4)	3 (5.8)	} 3 (8.6)	3 (4.7)	} 67 (67.7)	36 (69.2)	} 16 (45.7)	39 (60.9)
50 - 59		1 (4.2)		4 (8.5)		20 (83.3)		31 (65.9)
60+				2 (8.7)				20 (86.7)
Total	57 (8.2)	56 (8.7)	49 (10.1)	55 (7.4)	271 (51.8)	312 (41.1)	180 (37.1)	342 (45.9)

*Grossman *et al.* (1975)**Wasi *et al.* (1977)***Snitbhan *et al.* (1976a)****Scott *et al.* (1978)

to be no significant difference from prevalence of the general population.

HBsAg in various groups of population

Socioeconomic status and population density may also determine prevalence of HBV infection. A prevalence survey of HBsAg among various occupations found that HBsAg was detected in 4.4% of 778 merchants, 5.4% of 518 government officials, 7.2% of 166 students and 7.8% of 575 drug addicts (Kunarnage, 1983). Using radioimmunoassay technique, HBsAg was detected in 8.1% of 681 prostitutes (Scott *et al.*, 1974a). Prevalence of HBsAg among 472 prisoners was 5.1% (Urwijitaroon, 1982), but a higher prevalence of 20% was reported in another study of 50 prisoners (Sobeslavsky, 1975). A very low prevalence of 2% reported in

residents of a senile nursing home (Sobeslavsky, 1975) could be caused by seroconversion of HBsAg to anti-HBs in old age. Except for the studies in prisoners, the prevalence of HBsAg reported in various occupations and high risk groups ranges from 2% to 8.1% which is not higher than that of the general population.

Hepatitis B e antigen and antibody

Detection of hepatitis B e antigen (HBeAg) is of epidemiological importance because of its correlation with infectivity and development of chronicity. Prevalence surveys among HBsAg positive individuals revealed that 10% to 68.5% were positive for HBeAg and 1.7% to 38% were positive for anti-HBe (Table 3). The prevalence of HBeAg was highest in HBsAg asymptomatic carrier

Table 3
Prevalence of HBeAg and anti-HBe among HBsAg-positive sera.

Type of HBsAg-positive Sample	Sample size	Diagnostic procedure	HBeAg (%)	Anti-HBe (%)	Investigators (year of study)
Chronic active hepatitis	10	IEOP & ID	10	10	Chainuvati <i>et al.</i> , (1977)
Acute hepatitis	14	IEOP & ID	0	21.4	Chainuvati <i>et al.</i> , (1977)
Acute hepatitis (children)	43	ID	32.6	4.6	Pongpipat <i>et al.</i> , (1981)
Children with blood diseases	49	ID	53.1	8.2	Pongpipat <i>et al.</i> , (1981)
Asymptomatic carriers (age 0-14 yrs)	181	ID	68.5	1.7	Pongpipat <i>et al.</i> , (1981)
Asymptomatic pregnant carriers	110	ID	40.5	19.0	Pongpipat <i>et al.</i> , (1980)
Medical students	34	ID	55.9	5.9	Pongpipat <i>et al.</i> , (1979)
Blood donors	300	ID	40.7	18.3	Pongpipat <i>et al.</i> , (1982)
Blood donors	105	CIEP	14.3	4.3	Snitbhan <i>et al.</i> , (1976b)
Blood donors	260	ID	26.5	9.2	Urwijitaroon, (1982)

children (68.5%) but in children with icteric hepatitis B it was 34%. These results are similar to most reports from endemic countries but not to reports from low prevalence countries where HBeAg is not usually detected in asymptomatic HBsAg carriers. The e antigen system is of particular importance in maternal-fetus transmission as HBsAg positive mothers who carry HBeAg are of high infectivity to their babies. As high as 40% of HBeAg prevalence rate has been reported in Thai pregnant women with HBsAg (Pongpipat *et al.*, 1980).

Association between cirrhosis, hepatocellular carcinoma and hepatitis B

Chronic HBV infection can progress to cirrhosis and primary hepatocellular carcinoma (PHC). In Thailand, malignancy is the third most common cause of death

(Cancer statistics, 1971-1979) and PHC is the first and third most common carcinoma in male and female respectively (Szmunes, 1978; Srivatanakul and Sontipong, 1982). As shown in Table 4, about 6.1% to 75% of patients with PHC were reported to be HBsAg positive. In studies where sensitive assay techniques (RPHA, RIA) were used, a high prevalence of HBsAg in patients with PHC was reported and ranged from 34% to 75% (Pongpipat *et al.*, 1983a; Srivatanakul *et al.*, 1983). In histological studies of liver tissue by orcein stain, a reported prevalence of HBsAg ranged from 35% to 85% (Suwagoon, 1980; Panyathanya *et al.*, 1982; Bunyaratavej *et al.*, 1979) but only 4.0% to 12.5% of normal controls were positive for HBsAg (Bunyaratavej *et al.*, 1979; Panyathanya *et al.*, 1982). When compared to the prevalence of HBsAg in the

Table 4
Studies on the association between hepatocellular carcinoma (HCC)
and the hepatitis B virus in Thailand.

Investigators (year of study)	Diagnostic procedure	No. HBsAg positive/No. tested (%)			
		HCC with Cirrhosis	HCC not specified	Control	Others
Punyagupta <i>et al.</i> , (1973)	CFT & ID	12/24 (50.0)	15/60 (25.0)		
Benenson <i>et al.</i> , (1974)	CFT, IEOP & ID		1/11 (9.1)		
Chainuvati <i>et al.</i> , (1975)	CIEP	8/49 (16.3)**		2/87 (2.3)	
Thongcharoen <i>et al.</i> , (1976)	CIEP		2/33 (6.1)	40/400 (10.0)	Cirrhosis, 8/68 (11.8)
Phornphutkul and Peerakome (1982)	CIEP		12/40 (30.0)*	3/50 (6.0)	
Pongpipat <i>et al.</i> , (1983a)	RPHA		6/8 (75.0)		Hepatoblastoma 2/9 (22.0)
Srivatanakul <i>et al.</i> , (1983)	RIA		17/50 (34.0)*	5/50 (10.0)	Other liver diseases 22/50 (44.0)

*Diseases versus control, $p < 0.05$

**Diseases versus control, $p < 0.005$

general population, most studies show a higher prevalence of HBsAg among patients with cirrhosis or PHC or both.

Transmission of Hepatitis B Virus

HBV can be transmitted by both vertical and horizontal routes. Horizontal transmission is an important mode of spread in developed countries where contaminated blood and blood products are the major causative agents. In endemic countries, intrafamilial transmission through close contacts and vertical transmission are of particular importance.

Horizontal transmission of HBV

In Thailand, prevalence surveys have been conducted in various groups e.g. health care personnel, drug addicts, prisoners, prostitutes. With the limited data available, it is suggested that prevalence of HBsAg in these high risk groups is similar to that of the general population (see prevalence of HBsAg in various groups of population).

Post transfusion hepatitis

Blood transfusion is another important mode of HBV transmission. The extent to which blood transfusion contributes to the spread of HBV in a population depends on the prevalence of carrier state of the blood donors and quality of antigen screening prior to transfusion. As to the prevalence of HBsAg of blood donors in Thailand, reports from various studies are similar to prevalence of the general population and ranges from 4.4% to 9.2% (Vejjajiva *et al.*, 1971; Pongpipat *et al.*, 1971; Thongcharoen, 1976; Punyapupta *et al.*, 1973; Chiewsilp *et al.*, 1974a).

For post transfusion hepatitis, there have been only few reports in Thailand. In 1973 Punyapupta reported 46.9% of 49 patients receiving blood transfusion became seroposi-

tive for HBV but only one case developed icteric hepatitis.

Transmission of HBV by sexual contact

According to Scott *et al.*, (1974a), prevalence of HBsAg in 681 prostitutes was 8.1% but none of U.S. military service men who were known to have sexual contact with Thai service girls, became seropositive for HBsAg after 8 months of follow up. Although this data do not support the hypothesis of HBV transmission by sexual contact, more surveys are necessary before any conclusion can be made.

Intrafamilial transmission of hepatitis B

There have been a few studies in Thailand concerning intrafamilial transmission of hepatitis B. It was found that the proportion of families positive for HBsAg increased with family sizes and so did the proportion of HBsAg carriers in the positive families (Grossman *et al.*, 1975), in particular families of high titre HBsAg carriers with HBeAg (Pongpipat *et al.*, 1980; Bancroft *et al.*, 1976). In addition, subtypes of HBsAg were found to be consistent within the families (Grossman *et al.*, 1975). These findings support intrafamilial contact as an important means of HBV transmission.

Vertical transmission of hepatitis B

In developing countries, maternal-fetus transmission of HBV is believed to be one of the main factors contributing to the high prevalence of hepatitis B. It is known that infected newborns have a higher tendency to become chronic carriers than individuals contacting the disease in later life.

In Thailand, prevalence of HBsAg in pregnant women ranged from 4.6% to 7% (Chiewsilp *et al.*, 1974b; Scott *et al.*, 1974b; Pongpipat *et al.*, 1980). Thus, about 600,000 to 1,000,000 Thai women in the reproductive

age group could spread HBV vertically to their children. Most studies reported a higher chance of contacting HBV among infants born to HBsAg positive mothers when compared to infants born to HBsAg negative mothers (Bancroft *et al.*, 1976; Scott *et al.*, 1974b; Pongpipat *et al.*, 1980). Of these high risk infants, about 30% were reported to become HBsAg carrier (Pongpipat *et al.*, 1980; Scott *et al.*, 1974b) and about 48% developed evidence of HBV infection (Bancroft *et al.*, 1976). In addition to HBsAg, HBeAg has also been found to be strongly associated with HBV transmission between mothers and their infants. Development of HBs-antigenemia was noted in approximately 75% of infants born to HBsAg carrier mothers with HBeAg but only 0-40% of corresponding infants born to HBsAg carrier mothers without HBeAg became hepatitis B carriers (Pongpipat *et al.*, 1980; Bancroft *et al.*, 1976).

For prophylaxis against vertical transmission of HBV, clinical trials of Hepatitis B immune globulin (HBIG) and Hepatitis B vaccine have been conducted in Thai infants born to HBsAg and HBeAg positive mothers (Pongpipat *et al.*, 1983b; 1984). After one year of follow up, there was a reduction in HBsAg carrier rate of approximately 70% in those treated with HBIG and of approximately 56% in those treated with Hepatitis B vaccine. The estimated efficacy was 78.4% for HBIG and 60% for Hepatitis B vaccine.

SUMMARY

HBV infection is hyperendemic in Thailand. Approximately 5 million Thais are chronic HBV carriers. The prevalence of HBV markers in general population varies from 40-60%. Approximately 10-20% of children between the ages 1-5 years have serologic evidence of HBV infection and this prevalence increases with age reaching a plateau of 40-60% by age 20. High risk groups are

household contacts of HBsAg carriers and babies born to HBsAg positive mothers. Approximately 75% of the babies born to HBsAg & HBeAg positive mothers become HBsAg positive at 3 months after birth. A few studies showed that the HBV prevalence of hospital personnel and other high risk groups is similar to that of the general population. The prevalence of chronic HBsAg carrier varies from 5-10% and is highest among age groups 10-30 years.

Primary hepatocellular carcinoma (PHC) is the first and third most common cancer among Thai males and females, respectively. Approximately 35%-75% of PHC in adults are HBsAg positive. Histological studies showed that 47.3% of cryptogenic cirrhosis, 58%-66% of PHC and 35%-85% of cryptogenic cirrhosis with PHC were HBsAg positive.

Studies on Hepatitis B immune globulin and Hepatitis B vaccine revealed a 70% and 56%, respectively, reduction in the HBsAg prevalence of infants born to HBsAg and HBeAg positive mothers.

More epidemiologic, clinical and laboratory studies on HBV infection are being carried out by groups of scientists and investigators in the Ministry of Public Health and many medical schools. A national committee has been appointed to plan strategy for controlling HBV.

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