A SEROEPIDEMIOLOGICAL STUDY ON HEPATITIS B VIRUS, HEPATITIS C VIRUS AND HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN NORTHERN THAILAND

Prapan Jutavijittum¹, Yupa Jiviriyawat¹, Amnat Yousukh¹, Kan Toriyama², Hideyo Itakura², Michitami Yano³ and Shigeki Hayashi⁴

Received December 3, 1998/Accepted January 26, 1999

Abstract: A total of 1,889 voluntarily donated blood from five provinces in northern Thailand were investigated for the prevalences of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection. The average positive rates of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV were 8.7, 42.6, 0.5, 1.6 and 1.7%, respectively. The highest positive rates of HBs-Ag, anti-HBs, IgM anti-HCV and anti-HIV were found in the age group under 19 years (13.3%), 40-49 year old group (47.6%), 20-29 year old group (0.6%), 30-39 year old group (2.6%) and 20-29 year old group (2.9%), respectively. We found only two cases that were anti-HIV and HBs-Ag positive. There are no cases that were anti-HIV and IgM anti-HBc positive, and that were anti-HIV and anti-HCV positive. These results suggest that in northern Thailand, most of the HBV infections are due to vertical transmission from mother to child, although HBV infection is a major cause of viral hepatitis, HCV infection will become an important public health problem in the near future and that the prevalence of HIV infection is quite high among sexually active generations. Therefore, there is a need for more medical attention to these blood-borne virus diseases, and we strongly recommend routine blood screening for HCV in every medical institutions in northern Thailand.

Key words: HBV, HCV, HIV, northern Thailand

Introduction

Although HBV infection is highly endemic in Asia, Africa and Middle and South America, having harmful influences to the population in these countries, the introduction of routine donor blood screening for HBs-Ag has decreased the incidence of HBV infection in many of these countries. In Thailand, HCV infection has become the major cause of post-transfusion and sporadic hepatitis (Tanprasert *et al.*, 1993). The HIV infected population is increasing in northern Thailand and it is also well known that there are high prevalences of HBV and HCV infections among anti-HIV positive populations (Esteban *et al.*, 1989; Botti *et al.*, 1992; Eysler *et al.*, 1993; Bryan *et al.*, 1993; Yousukh *et al.*, 1996). However the seroepidemiological study of

the correlation among these viral infections have not been well established in northern Thailand. It is the purpose of this study to determine the prevalences of HBV, HCV and HIV infections among voluntarily donated bloods and discuss the transmission routes to formulate prevention strategies of these blood-borne virus infections in northern Thailand.

MATERIALS AND METHODS

The total number of 1,889 serum samples were randomly collected from the voluntary blood donors at Chiang Mai University Hospital and Chiang Rai, Lampang, Lamphun and Phayao Provincial Hospitals in northern Thailand (Fig. 1) during June to December, 1995 and stored at -20° C until examination. Sera were

^{1.} Department of Pathology, Faculty of Medicine, Chiang Mai University, 110 Intavaroros Rd., Chiang Mai 50200, Thailand

^{2.} Department of Pathology, Institute of Tropical Medicine, Nagasaki University, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan

^{3.} Institute for Clinical Research, Nagasaki Chuo Hospital, 2-1001-1 Kubara, Omura 856-0835, Japan

^{4.} Department of Gastroenterology, International Medical Center of Japan, 1-21-1 Toyama, Shinjuku 162-8655, Tokyo, Japan



Figure 1 Map of northern Thailand

tested for the presence of HBs-Ag by using *Auszyme Monoclonal* (the third generation EIA kit, Abbott Lab. Ltd., North Chicago, Illinois, USA), anti-HBs by *Ausab EIA* (human-subtypes ad and ay, Abbott Lab. Ltd., North Chicago, Illinois, USA) and the anti-HBs titers of positive samples were calculated and seroprotection was defined as anti-HBs levels ≥ 10 mIU/ml (Andre, 1989; Yap $et\ al.$, 1992), IgM anti-HBc by Corzyme-M (γ DNA, Abbott Lab. Ltd., North Chicago, Illinois, USA), anti-HCV by $Abbott\ HCV\ EIA\ 3.0\ (c100-3,\ HC-34,\ HC-43,\ NS5,\ Abbott\ Lab.\ Ltd.,\ North\ Chicago,\ Illinois,\ USA)$ and anti-HIV by $Abbott\ Recombinant\ HIV-1/HIV-2$ (the third generation EIA kit, Abbott Lab. Ltd., North Chicago, Illinois, USA). The statistical analysis of the results was performed using chi-square test.

RESULTS

Table 1 shows the prevalence of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV in 1,889

voluntary blood donors from five provinces of northern Thailand. The average positive rates are 8.7% for HBs-Ag, 42.6% for anti-HBs, 0.5% for IgM anti-HBc, 1.6% for anti-HCV and 1.7% for anti-HIV. The highest rates of HBs-Ag, anti-HCV and anti-HIV positive are found to be 10.9%, 2.5%, and 2.5% respectively, in Phayao and anti-HBs of 46.4% and IgM anti-HBc of 1.2% in Lamphun.

Table 2 summerizes the age distribution of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV positive among the blood donors. The highest positive rates of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV were found to be 13.3% in the group under 19 years old, 47.6% in the 40-49 year age group, 1.6% in the 20-29 year old group, 2.6% in the 30-39 year old group and 2.9% in the 20-29 year old group, respectively.

The prevalence of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV among male donors is described in Table 3. The average positive rates were 9.8% for HBs-Ag, 44.0% for anti-HBs, 0.4% for IgM anti-HBc, 2.1% for anti-HCV and 1.6% for anti-HIV. The highest positive rate of HBs-Ag of 14.7% was found in the under 19 year old group, anti-HBs of 52.7% in the 30-39 year old group, IgM anti-HBc of 0.9% in the 20-29 year old group, anti-HCV of 3.6% in the 30-39 year old group and anti-HIV of 2.7% in the 20-29 year old group.

The prevalence of HBs-Ag, anti-HBs, IgM anti-HBc, anti-HCV and anti-HIV positive among female donors is represented in Table 4. The average positive rates were 6.5% for HBs-Ag, 39.4% for anti-HBs, 0.8% for IgM anti-HBc, 0.7% for anti-HCV and 1.8% for

Table 1	Prevalence of HBV, HCV	' and HIV	infections in	five	provinces	in northern	Thailand

Provinces	Number	HBs-Ag	HBs-Ab	IgM anti-HBc	anti-HCV	anti-HIV
Chiang Mai	390	20 (5.1%)	161 (41.3%)	2 (0.5%)	3 (0.9%)	6 (1.5%)
Chiang Rai	415	42 (10.1%)	167 (40.2%)	3 (0.7%)	7 (1.7%)	8 (1.9%)
Lampang	380	37 (9.7%)	150 (39.5%)	0 (0.0%)	7 (1.8%)	2 (0.6%)
Lamphun	345	27 (7.8%)	160 (46.4%)	4 (1.2%)	5 (1.5%)	7 (2.0%)
Phayao	359	39 (10.9%)	166 (46.2%)	1 (0.3%)	9 (2.5%)	9 (2.5%)
Total	1,889	165 (8.7%)	804 (42.6%)	10 (0.5%)	31 (1.6%)	32 (1.7%)

Table 2 Prevalence of HBV, HCV and HIV infections by age in northern Thailand

Age (years)	Number	HBs-Ag	HBs-Ab	IgM anti-HBc	anti-HCV	anti-HIV
≦19	248	33 (13.3%)	92 (37.1%)	1 (0.4%)	0 (0.0%)	4 (1.6%)
20-29	447	36 (8.1%)	156 (34.9%)	7 (1.6%)	7 (1.6%)	13 (2.9%)
30-39	547	43 (7.9%)	256 (46.8%)	2 (0.4%)	14 (2.6%)	10 (1.8%)
40-49	382	35 (9.2%)	182 (47.6%)	0 (0.0%)	6 (1.6%)	5 (1.3%)
≥50	265	18 (6.8%)	118 (44.5%)	0 (0.0%)	4 (1.5%)	0 (0.0%)
Total	1,889	165 (8.7%)	804 (42.6%)	10 (0.5%)	31 (1.6%)	32 (1.7%)

anti-HIV. The highest rates of HBs-Ag of 8.8% was detected in under 19 year old group, anti-HBs of 48.0% in the 40-49 year old group, IgM anti-HBc of 3.6% in the 20-29 years old group, anti-HCV of 1.8% in the 20-29 year old group and anti-HIV of 3.6% in the 20-29 year old group.

Table 5 demonstrates the anti-HBs levels of 804 anti-HBs positive cases. 727 out of 804 anti-HBs positive cases (90.4%) had the seroprotection level of anti-HBs ($\geq 10 \text{ mIU/m}l$) and 77 cases (9.6%) showed the levels less than 10 mIU/ml. The highest prevalence (94.9%) of protection levels $\geq 10 \text{ mIU/m}l$ was found in the 20-29 year old group.

DISCUSSION

According to the classification by WHO (Zuckerman, 1987), Thailand belongs to an intermediate prevalence region group of HBV infection (2–7.9%) and the previous report revealed that the average prevalence of HBs-Ag is 7.4% among the donated blood between 1970

and 1980 in central Thailand (Chainuvati et al., 1990). Our result of 8.7% positive among the voluntary donated blood in 1995 from five provincial areas of norhtern Thailand is similar to the previous report of 7.9% positive in 1991 in Chiang Mai (Yousukh et al., 1996). These findings suggest that the prevalence of HBs-Ag positive in northern Thailand differs little from that of central Thailand. There is a slight difference in the prevalence of HBs-Ag positive between 9.8% in male and 6.5% in female (p<0.05) and also in the prevalence of anti-HBs positive between 44.0% in male and 39.4% in female (p<0.05). The reason for the higher HBV infection rate in male than female is unclear. However it is suspected that males have higher risk of contacting HBV than females, possibly via sexually transmitted route in Thailand (Tanprasert et al., 1993). younger age group under 19 years old shows the highest rate of HBs-Ag positivie and the lowest rate is found in the age group over 50 years. Contrary to the rate of HBs-Ag positive, a higher rate of anti-HBs is found among the older age groups. In regard to the protective

Table 3 Prevalence of HBV, HCV and HIV infections among male donors in northern Thailand

Age (years)	Number	HBs-Ag	HBs-Ab	IgM anti-HBc	anti-HCV	anti-HIV
nge (years)	TAUTIDEL		11103-110	igni anti HDC	and 110 v	
≤ 19	191	28 (14.7%)	70 (36.6%)	1 (0.5%)	0 (0.0%)	2 (1.0%)
20-29	336	33 (9.8%)	118 (35.1%)	3 (0.9%)	5 (1.5%)	9 (2.7%)
30-39	366	30 (8.2%)	193 (52.7%)	1 (0.3%)	13 (3.6%)	7 (1.9%)
40-49	257	27 (10.5%)	122 (47.5%)	0 (0.0%)	6 (2.3%)	3 (1.2%)
≥50	147	8 (5.6%)	66 (46.5%)	0 (0.0%)	3 (2.1%)	0 (0.0%)
Total	1,292	126 (9.8%)	569 (44.0%)	5 (0.4%)	27 (2.1%)	21 (1.6%)

Table 4 Prevalence of HBV, HCV and HIV infections among female donors in northern Thailand

Age(years)	Number	HBs-Ag	HBs-Ab	IgM anti-HBc	anti-HCV	anti-HIV
≤19	57	5 (8.8%)	22 (38.6%)	0 (0.0%)	0 (0.0%)	2 (3.5%)
20-29	111	3 (2.7%)	38 (34.2%)	4 (3.6%)	2 (1.8%)	4 (3.6%)
30-39	181	13 (7.2%)	63 (34.8%)	1 (0.6%)	1 (0.6%)	3 (1.7%)
40-49	125	8 (6.4%)	60 (48.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)
≥ 50	123	10 (8.1%)	52 (42.3%)	0 (0.0%)	1 (0.8%)	0 (0.0%)
Total	597	39 (6.5%)	235 (39.4%)	5 (0.8%)	4 (0.7%)	11 (1.8%)

Table 5 Anti-HBs levels by age and sex in northern Thailand

Age (years)	Ma	ale	Fen	nale	Total	
	≥10 mIU/m <i>l</i>	<10 mIU/m <i>l</i>	≥10 mIU/m <i>l</i>	<10 mIU/m <i>l</i>	≥10 mIU/m <i>l</i>	<10 mIU/m <i>l</i>
<u>≤19</u>	61 (87.1%)	9 (12.9%)	21 (95.5%)	1 (4.5%)	82 (89.1%)	10 (10.9%)
20-29	112 (94.9%)	6 (5.1%)	36 (94.7%)	2 (1.8%)	148 (94.9%)	8 (5.1%)
30 - 39	175 (90.7%)	18 (9.3%)	58 (92.1%)	5 (7.9%)	233 (91.0%)	23 (9.0%)
40-49	111 (91.0%)	11 (9.0%)	52 (86.7%)	8 (13.3%)	163 (89.6%)	19 (10.4%)
≥ 50	57 (86.4%)	9 (13.6%)	44 (84.6%)	8 (15.4%)	101 (85.6%)	17 (14.4%)
Total	516 (90.7%)	53 (9.3%)	211 (89.8%)	24 (10.2%)	727 (90.4%)	77 (9.6%)

anti-HBs level more than 10 mlU/ml, the highest prevalence rate was found in the 20–29 year old group and the rate steadily decreased with increasing age. In addition, the rate of IgM anti-HBc positive, which indicates acute or recent HBV infection, usually within six months or less, is 0.5% among the total donated blood. These findings suggest that the main transmission route of HBV infection is a vertical infection during the neonatal period, however there are some occurrences of the horizontal infection of HBV in northern Thailand.

The screening tests for anti-HCV in blood donors using the 2nd generation EIA test, revealed 1.6% of anti-HCV positive in Bangkok (Nuchprayoon et al., 1993), 1.3% in Khon Kaen, north eastern Thailand (Tomanakan. 1994) and 2.4% in Chiang Mai (Hotta et al., 1997). Our results using the 3rd generation EIA test which provides an improved sensitivity for the detection of anti-HCV seroconversion and the identification of HCV infected individuals showed 1.6% of anti-HCV positive among the donated blood. It has been suggested that artificial factors such as reusing syringes for some vaccination, which is contaminated with HCV are the main reasons for the higher prevalence in older people in Japan (Yano, 1992). The fact that the prevalence of HCV infection is the highest in the 30-39 year old group, and no positive case is found in the age group under 19 years old, may indicate that the similar factors play a role in the transmission of HCV among the specified age group in northern Thailand.

Since 1988, Thailand has witnessed an explosive rise in the number of HIV-infected populations (Phanuphak et al., 1995). In particular, prevalence is the highest in the Upper North. Ungchusak et al. (1995) reported the result of their serosurveillance for HIV infection of donated blood in Thailand; the median prevalence is 0.77% in northern Thailand; 1.56% in Chiang Rai, 2.3% in Phayao, 1.47% in Chiang Mai, 0.77% in Lampang and 3.24% in Lamphun. Our results are similar to their findings. Sexually active generations in their 20's show higher positive rates of anti-HIV. Phayao and Lamphun have higher rates of HIV infection, 2.5 and 2.0%, respectively, and Lampang shows the lowest rate at 0.6%. The reason for the differences in these geographic features has not been determined. More intensive studies are needed to find the reasons of these differences, especially on geographical and ecological aspects.

It is well known that there is a high prevalence of HBV and HCV infection among HIV positive individuals (Esteban *et al.*, 1989; Botti *et al.*, 1992; Eysler *et al.*, 1993; Bryan *et al.*, 1993; Quan *et al.*, 1993; Yousukh *et al.*, 1996), however, we found only 2 cases that are HBs-

Ag and anti-HIV positive and no cases that are IgM anti-HBV and anti-HIV positive, and anti-HCV and anti-HIV positive in the present study. Further investigation is necessary to confirm these findings.

The results of our study suggest as follows; 1) Although there are some occurences of horizontal infection, the transmission route of HBV infection is mainly due to vertical infection in northern Thailand and it is important to prevent HBV infection from HBs-Ag positive mother to infant, 2) Although HCV infection is less prevalent than HBV infection at present, it will become an important public health problem in the near future, and it is strongly recommended to introduce routine screening of anti-HCV in the donated blood, 3) The incidence of HIV infection is quite high in northern Thailand and it will need more medical attention.

ACKNOWLEDGMENTS

We are grateful to the relevant officers in Chiang Rai, Lampang, Lamphun and Phayao Provincial Hospitals for their cooperation. This work was supported by a Grant for International Health Cooperation Research (9C-4) from the Ministry of Health and Welfare, Japan.

REFERENCES

- 1) Andre, F.E. (1989): Summary of safety and efficacy data on a yeast-derived hepatitis B vaccine. Am. J. Med., 87 (Suppl. 3A), 14S-20S
- Botti, P., Pistelli, A., Gangassi, F., Zorn, A.M., Caremelli, L., Peruzzi, S., Smorlesi, C., Masini, E. and Mannaioni, P.F. (1992): HBV and HCV infection in i.v. drug addicts; coinfection with HIV. Arch. Virol. Supple. 4, 329-332
- Bryan, J.P, Sjogren, M.H., Malone, J.L. Macarthy, P., Kao, T.C., Wagner, K., Sheffield, J., Smith, E. and Perine, P.L. (1993): Recombinant immunoblot assays for hepatitis C in human immunodeficiency virus type 1injected US navy personnel. J. Infect. Dis., 167 (3), 715-716
- 4) Chainuvati, T. (1990): Epidemiology of hepatitis B virus infection in Asian countries, outlook in Thailand. *In* Hepatitis infection, current status and recent development. (eds. Chan Soh Ha), Melirwin Enterprises, Singapore, 99-104
- 5) Esteban, J.I., Esteban, R., Viladomiu, L., Lopez-Talavera, J.C., Hernandez, J.M., Raget, M., Vargas, V., Gienesa, J., Buti, M., Guardia, J., Houghton, M., Choo, Q. L. and Kuo, G. (1989): Hepatitis antibodies among risk groups in Spain. Lancet, 2, 294–297
- Eysler, M.E., Diamondstone, L.S., Lien, J.M., Ehmann, W.C., Quan, S. and Goedert, J.J. (1993): Natural history

- of hepatitis C virus infection in multitransfused hemophiliacs; effect of coinfection with human immunodeficiency virus. The multicenter Hemophilia Cohort Study. J. AIDS, 6(6), 602-610
- Hotta, H., Kemapunmanus, M., Apichartpiyakul, C., Soetjipto, Handajani, R. and Barzaga, N.G. (1997): Differential distribution of hepatitis C virus subtypes in Asia: Comparative study among Thailand, Indonesia, the Philippines and Japan. Southeast Asian J. Trop. Med. Publ. Health, 28 (Suppl. 3), 23-31
- 8) Nuchaprayoon, T., Somjitta, S., Adulwijit, S. and Chumnijarakij, T. (1993): Hepatitis C virus antibody in blood donors. Chula. Med. J., 37 (7), 443-449
- 9) Phanuphak, P., Locharernkul, C., Panmuong, W. and Wilde, H. (1995): A report of three cases of AIDS in Thailand. Asian Pacific J. Allergy and Immunol., 3(2), 195–199
- 10) Quan, C.M., Krajden, M., Grigoriew, G.A. and Salit, J.E. (1993): Hepatitis C virus infection in patients infected with the human immunodeficiency virus. Clin. Infect. Dis. 17 (1), 117–119
- 11) Tanprasert, S., Somjitta, S. and Preechakul, L. (1993): Three-year trend for HBs-Ag screening in donated blood; National Blood Center, Thai Red Cross Society.

- Chula. Med. J., 37(2), 111-117
- 12) Tomanakan, K. (1994): Prevalence of anti-HCV in voluntary blood donors at Khon Kaen Hospital. Thai J. Hematol. Transf. Med., 4(2), 113-116
- 13) Ungchusak, K., Tonghong, A., Sangwonly, O., Thepsittha, K., Rujuvipat, V. and Jansiriyakorn, S. (1995): The 13th round of HIV sentinel serosurveillance in Thailand. Thai AIDS J., 7(4), 177–189 (in Thai with English abstract)
- 14) Yano, M. (1992): Editorial comment; Advance in hepatitis C; Sero-epidemiology and natural history. J. Gastroenterol. Hepatol., 7, 43-44
- 15) Yap, I., Guan, R. and Chan, H. (1992): Recombinant DNA hepatitis B vaccine containing pre-S components of the HBV coat protein; a preliminary study on immunogenicity. Vaccine, 10, 439-442
- 16) Yousukh, A., Toriyama, K., Jutavijittum, P., Jiviriyawat, Y., Mundee, Y., Phornphutkul, K., Kusuda, M. and Itakura, H. (1996): A high prevalence of hepatitis C virus infection among the human immunodeficiency virus seropositive blood donors in Chiang Mai, Thailand. Trop. Med., 38(1), 21-25
- 17) Zuckerman, A.J. (1987): The development of novel hepatitis B vaccines. Bull. W.H.O., 65, 265-275