HEPATITIS B AND C VIRUS INFECTION PREVALENCE AMONG WOMEN IN MANILA, THE PHILIPPINES

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Abstract. A seroepidemiological survey of HBsAg, HBeAg, anti-HBs, anti-HBc, anti-HBe and anti-HCV positivities was conducted in 1997 in Manila, The Philippines. Adult women (21 to 59 years of age) were invited to donate peripheral blood for the study, and 50 people volunteered. They were nonsmokers, nonhabitual drinkers, and mostly married; none of them was a professional blood donor. The serum assay showed that all subjects were negative for HBsAg and HBeAg. Overall, a half (50%) of the study subjects were positive for any one of the HBV infection markers (*ie* HBV^+). The older group (25 women at 36-59 years of age) showed significantly higher prevalence than the younger group (25 women at 21-35 years of age) of positivity to all three HBV antibody markers and therefore HBV positivity also. None of the study subjects was positive for anti-HCV. Comparison of the present findings with the results reported in the literature for the 1980s suggests that the risk of HBV infection and most probably that of HCV infection also has decreased in this 10-year period in the Philippines.

INTRODUCTION

Infections of hepatitis B and C viruses (to be abbreviated as HBV and HCV, respectively) are two risk factors of hepatocellular carcinoma (HCC) in many Asian countries (Lingao *et al,* 1981; Yuki *et al,* 1992; Okuno *et al,* 1994; Tsai *et al,* 1994; Di Bisceglie, 1995; Mansell and Locarnini, 1995). The prevalence of these diseases in The Philippines was a focus of attention of several medical groups in the 1980s (Lingao *et al,* 1981; Basaca-Sevilla *et al,* 1986; Lingao *et al,* 1986); the situations in the 1980s were recently reviewed and high risk groups were identified (Lansang, 1996). It appears likely however that studies are rather scarce in 1990s in the Phillpines, especially on the prevalence of HBV and HCV infection, among the general population (Mansell and Locarnini 1995; Lansang 1996).

A small scale survey was conducted by this joint study group on an exploratory basis to assess the current situation among the citizens in Manila, the Philippines. The study results are presented in this communication.

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MATERIALS AND METHODS

Study population and study design

A seroepidemiological survey was conducted in June, 1997, in the city of Manila. Adult women (21 to 59 years of age) in the clerical section of a large medical complex were invited to join the study, and asked to offer peripheral blood samples: 50 people volunteered. A medical interview revealed that they were nonsmokers, nonhabitual drinkers, and mostly married; none of them was a professional blood donor. Blood samples were drawn from the cubital vein.

The small size of the survey, 50 subjects only, was taken into consideration in the study design. Accordingly, only one sex (women) was selected to exclude possible confounding effects due to the sex difference in infection prevalence, because a difference in HCC prevalence between two sexes is known to exist (Yuan *et al,* 1995).

Assay for markers of hepatitis virus B and C infection, and liver function

Assays for HBV and HCV infection markers were by commercial RIA or EIA kits, *ie* HBV surface antigen (HBsAg) by AUSRIA II-125, HBV envelope antigen (HBeAg) by HBe RIAKIT II, HBV core antibody (anti-HBc) by RIAKIT, HBV surface antibody (anti-HBs) by AUSAB, HBV envelope antibody (anti-HBe) by HBe RIAKIT II, and HCV antibody (anti-HCV) by HCV EIA II (all from Abbott-Dianabott, Tokyo, Japan). The criteria for evaluation of the assay results are summarized in Table 1. Three serum enzyme activities [aspartate aminotransferase (ASAT: EC 2.6.1.1), alanine aminotransferase (ALAT: EC 2.6.1.2), γ-glutamyl transpeptidase (γ-GTP: EC 2.3.2.1)] were assayed by conventional methods.

Statistical analysis

A log-normal distribution was assumed for serum enzyme activities so that geometric means (GMs) together with geometric standard deviations (GSDs) were calculated. Unpaired *t*-test (after logarithmic conversion) and chi-square test were employed for detection of difference in means and prevalence, respectively.

RESULTS

Positivity for hepatitis virus infection markers

The results of assays on HBV and HCV infection markers are summarized in Table 2 in terms of numbers of positive cases and also borderline cases. It is interesting to note that all subjects were negative for HBsAg and HBeAg. Positivity for antibodies varied depending on the antibody assayed; the prevalence was highest with anti-HBs$^+$. All anti-HBc$^+$ cases were also positive for anti-HBs. All anti-HBe$^+$ cases were positive for both anti -HBs and anti-HBc. Overall, half (50%) of the study subjects were positive at least for one of the HBV infection markers (*ie* HBV$^+$), but none of them were antigen-positive, as stated above.

When the subjects were classified by age into two groups of an equal size (*ie* one group of 25 women at 21-35 years of age and the other group of 25 women at 36-59 years of age) and the prevalence was compared by chi-square test (Table 2), it was found that the older group showed significantly ($p<0.05$) higher prevalence than the younger group in positivity for all three antibody markers and therefore HBV-positivity. This higher prevalence in markers still stood when the positive and border-

Table 1

Criteria for hepatitis B and C virus infection markers.

Indicative of hepatitis virus infection	Unit	Criteria		
		Negative	Borderline	Positive
Hepatitis B				
HBsAg	Cut-off ratio	< 1	≥ 1 to < 5	≥ 5
HBeAg	Cut-off ratio	< 1	≥ 1 to < 2	≥ 2
Anti-HBs	Cut-off ratio	< 1	≥ 1 to < 2	≥ 2
Anti-HBc	Suppression	< 30%	≥30% to <70%	≥70%
Anti-HBe	Suppression	< 30%	≥30% to <70%	≥70%
Hepatitis C				
Anti-HCV	Cut-off index	< 1	–	≥ 1

Abbreviations are: HBsAg, HBV surface antigen; HBeAg, HBV envelope antigen; anti-HBs, HBV surface antibody; anti-HBc, HBV core antibody; anti-HBe, HBV envelope antibody; anti-HCV, HCV antibody.

Table 2

Prevalence of hepatitis B and C virus infection markers by age group.

Indicative of hepatitis virus infection	Age range (years)		
	21-35	36-59	Total
Number of cases	25	25	50
Hepatitis B			
HBsAg$^+$	0 (0)	0 (0)	0 (0)
HBeAg$^+$	0 (0)	0 (0)	0 (0)
Anti-HBs$^+$	8 (2)	16^a (1)^b	24 (3)
Anti-HBc$^+$	4 (1)	10^a (3)^b	14 (4)
Anti-HBe$^+$	1 (1)	6^a (5)^c	7 (6)
HBV$^+$	8 (2)	17^a (0)^b	25 (2)
Hepatitis C			
Anti-HCV$^+$	0 (0)	0 (0)	0 (0)

Abbreviations are as under Table 1.

Values are the number of positive cases (borderline cases in parentheses). Symbols (asterisks for positive cases, and daggers for positive cases + borderline cases) show that the difference from the values for the 20-35 year-old group is statistically significant (^{a}and^b for $p < 0.05$, and ^{c} for $p < 0.01$ respectively).

line positive cases were combined for evaluation. Further classification of the subjects by decade of ages (*ie* 12 women in the 20's, 19 women in the 30's, 13 women in the 40's and 6 women in the 50's) also showed that the prevalence of HBV$^+$ cases (positive and borderline cases in combination in parentheses) increased by age from 25% (33%) in the 20's to 53% (58%) in the 30's and to 69% (69%) in the 40's, although there was no further increase in the 50's, where only 6 cases were available. The difference of the prevalence among the 4 decades was statistically significant when examined by chi-square test ($p<0.05$ in both cases).

Another point of interest concerned HCV. None of the study subjects was positive for anti-HCV, and therefore statistical analysis to detect possible age-dependent differences could not be carried out (Table 2).

Serum enzyme activities in relation to HBV infection markers

The 50 cases were classified depending on the positivity for each marker, *ie*, the marker-positive group and the marker-negative (including borderline cases) group, and the activities of ASAT, ALAT and γ-GTP were compared between the two groups with an assumption of log-normal distribution (Table 3). Comparison by *t*-test showed that there was no significant ($p>0.10$) difference in the activities of the three enzymes between the two groups. Inclusion of the borderline cases in marker-positive groups did not result in changes in the conclusion.

When examined on an individual basis, two women showed subclinical increases in ASAT and ALAT activities together, *ie* a woman (59 year-old) showed 42 IU/l ASAT and 66 IU/l ALAT, and another woman (31 year-old) had 43 IU/l ASAT and 39 IU/l ALAT. Both of them were however negative for all HBV infection markers *(ie* HBV$^-$). Two other women with 44 IU/l ALAT (but with ASAT in the normal range, *ie* 32 and 39 IU/l, respectively) were also HBV$^-$. A 25 year-old woman with slightly elevated ALAT (55 IU/l) but with normal ASAT (28 IU/l) was positive for anti-HBs (although negative for all other four HBV infection markers). It should be added that none of the 50

Table 3

Serum enzyme activity by positivity for HBV infection markers.

HBV infection marker	Pos/neg	No. of cases	Serum enzyme activity (IU)		
			ASAT[a]	ALAT[b]	γ-GTP[c]
Anti-HBs	Positive	24	17.4 (1.33)	17.2 (1.67)	15.8 (1.62)
	Negative[d]	26	20.1 (1.39)	18.7 (1.77)	14.7 (1.72)
Anti-HBc	Positive	14	18.9 (1.33)	18.7 (1.65)	15.9 (1.75)
	Negative	36	18.7 (1.39)	17.7 (1.75)	15.0 (1.64)
Anti-HBe	Positive	7	19.2 (1.39)	18.8 (1.80)	15.3 (1.79)
	Negative	43	18.7 (1.37)	17.8 (1.71)	15.2 (1.66)
HBV	Positive	25	17.4 (1.32)	17.0 (1.66)	15.5 (1.62)
	Negative	25	20.3 (1.40)	18.9 (1.78)	14.9 (1.73)

Abbreviations are as under Table 1.

Unless otherwise specified, values are GM (GSD) of enzyme activity. There was no statistically significant difference between the positive and negative cases ($p>0.10$).

[a] ASAT; aspartate aminotransferase.

[b] ALAT; alanine aminotransferase.

[c] γ-GTP; γ-glutamyl transpeptidase.

[d] Including borderline cases.

women reported a past history of hepatitis.

DISCUSSION

From the present survey of 50 adult women in Manila, it is possible to summarize that none of the study subjects were positive for HBsAg, HBeAg, or anti-HCV. Overall positivity for HBV infection was 50%, and the prevalence of the positive cases was higher in the 36-59 year-old people than in the 21-35 year-old people in antibody markers, when the positivity for the marker was evaluated separately, and therefore in combination. Thus, the prevalence of HBV^+ cases was 68% in the older group, and 32% in the younger group.

It is of public health interest to know when the HBV infection of those positive for antibody markers (*ie* 50% of the women studied) took place. Vertical transmission at the very early stage of life is unlikely; if vertical, the infection occurred when the subjects were quite young and their immune system was still immature, and therefore at least some of the subjects would be expected to remain antigen-positive in their adulthood. Horizontal transmission among young siblings is also unlikely for the same reason. Although infection at the later stage of life may be possible, none had a past history of hepatitis. Thus, it is not possible to reach any answers at this point in the study.

The study subjects were recruited from staff in a medical complex. Although the medical profession (especially clinical laboratory staff and nurses) is a known high risk factor of HBV and HCV infection (Byrne 1966; Nishimura *et al,* 1990), the job of present study subjects was desk work in a clerical section with no direct contact with patients, and therefore their risk of HBV and HCV infection should be no higher than that of the general population.

Regarding HBV infection prevalence among the general population in the Philippines, Lingao *et al* (1981) reported that the HBV^+ prevalence among 84 subjects (examined as age-matched controls to

HCC cases) was 57%, and that of HBsAg$^+$ was 18%. The HBeAg-positivity was 2%. Lingao *et al* (1986) studied also rural populations and found that the HBV$^+$ and HBsAg$^+$ prevalence was 58% and 12%, respectively, for whole populations which consisted of both children and adults. The prevalence of HBV$^+$ cases increased by age, *ie* from 59-75% at 20-29 years of age (various among 4 rural populations) to reach a peak of 78-98% at 40-49 years, whereas HBsAg$^+$ prevalence showed a peak of 20-23% at the ages below 10 years in 2 populations and 22-26% at 20-49 years in the remaining two populations. According to Basaca-Sevilla *et al* (1986), HbsAg$^+$ varied among populations studied in a range of 10-16% and that of anti-HBs$^+$ in Ag$^+$ 45-50%. For example, the HBsAg+ prevalence in the general population in Metro Manila, people in rural areas and military academy cadets was 11.8%, 10.9% and 10.1%, respectively. The highest HBsAg$^+$ prevalence of 16% was recorded in a minority tribe in the mountains.

Arguillas and others (1991) studied HBV infection among blood donors (whether the donors were professionals or volunteers was not stated) and medical staff. The HBsAg$^+$ prevalence was 2.2% and 6.5%, and that of the HBV$^+$ cases was 63.5% and 72.3% among the donors and the medical staff, respectively. In this connection, it is of interest to note that the urban-rural comparison of the data suggest that the HBsAg$^+$ prevalence appears to be higher in cities than in villages in the Philippines (*eg* Basaca-Sevilla *et al,* 1986), contrary to the case in China where the HBsAg$^+$ prevalence was higher in rural areas than in urban areas (Yao, 1996). Compared with such prevalence in 1980s, the present observation of 0% for HBsAg$^+$ and 50% for HBV$^+$ (Table 2), although based on a small sample, suggests that there was substantial decrease in HBV infection risk in the last decade. The observation that the HBV$^+$ prevalence is lower among younger people than among older people (Table 2) is in line with the conclusion of decreased HBV infection risk.

No anti-HCV$^+$ case was detected among the 50 subjects in the present study (Table 2). Reports published on HCV infection prevalence in the Philippines are limited. Thus, Arguillas *et al* (1991) reported that blood donors (with no description whether or not they were professional) and medical staff showed HCV$^+$ prevalence of 2.2 and 1.6%, respectively, when anti-HCV (anti C100-3) was assayed [according to the study results by Iino *et al* (1991), the sensitivity of the method used by Arguillas *et al* (1991) appears to be comparable to the method used in the present study].

In other areas in Asia, an anti-HCV$^+$ prevalence of 2.2% and 2.4% was reported for general populations in northern and southern Taiwan, respectively (Liu *et al,* 1991; Tsai *et al,* 1994). The prevalence was 2.1% in the northern part of China (Tao *et al,* 1991) and 1.3% in Tokyo, Japan (Watanabe *et al,* 1990). In the Tokyo study, the anti-HCV$^+$ tended to increase at advanced ages, but the number of positive cases was too small to allow statistical evaluation, although it was clear that there was no sex difference in the prevalence (Watanabe *et al,* 1990). The number of cases examined in the present study is not sufficient to allow statistical comparison with these data.

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