ORIGINAL CONTRIBUTION

Prevalence of Hepatitis B Virus infection Markers Among a Working Population in a Coastal City of Yantai, China

Kazunori Seiji¹, Masaru Takahashi², Osamu Inoue³, Shi-Xiong Cai²
Mei-Yuan Huang², Takao Watanabe³, Toshio Kawai⁴, Tomojiro Yasugi⁴
Jiang-Bin Qu⁵, and Masayuki Ikeda⁶

Three markers of hepatitis B virus (HBV) infection, HBsAg, anti-HBs and anti-HBc, were investigated in the sera from 426 factory workers of both sexes in a coastal city of Yantai in China. The investigation showed that the rate of those positive to HBsAg was 25.4% (25.9% in men and 24.6% in women), and that the rate when two sexes were combined was highest (i.e., 29.5%) at the ages of 20s followed by gradual decrease at higher ages (below 20%). The over-all HBV infection rate as calculated by those positive to any of the three markers studied was 70.4%. Comparison with rates reported in literature indicated that the rate of HBsAg-positive cases in the present study are probably among the highest values in China, whereas over-all rate of HBV infection was almost comparable to the values for other provinces. It should be added that other reports on other parts of Shandong Province describe HBsAg prevalence of about 6%. No explanation is currently available for the high HBsAg prevalence among the study population. *J Epidemiol*, 1991; 1: 11-17.

anti-HBc, anti-HBs, China, HBsAg, HBV

Persistent infection of hepatitis B virus (HBV) is among the known risk factors of primary hepatocellular carcinoma (PHC). Accordingly, increasing attention has been given in public health to the prevalence of the HBV infection with intention for the prevention of this insidious disease¹⁻⁷. It is generally understood that the prevalence is higher in many parts of the Asian and Pacific regions than in northern Europe and North America^{1,2,4,8-10}. Reports on HBV prevalence in China are also growing in numbers in recent years reflecting the large population, with focus to the areas of high PHC incidence such as Guangxi Province^{8,7,11-15}.

In continuation of seroepidemiological surveys by this study group on HBV infection in East Asia¹⁶⁻¹⁹, a study was conducted in a coastal city of Yantai in Shandong Province, China, the area where there still

exists a paucity of data on HBV infection.

MATERIALS AND METHODS

Sera. In 1991, the survey was conducted in a port city of Yantai in Shandong Province, on the north coast of the Shandong Peninsula, as a part of an occupational health survey of factory workers. The workers both in production sections and in clerical sections were invited to participate in the study, and sera obtained from 426 workers (243 men and 183 women at the ages of 17 to over 50 years) were subjected to the sero-epidemiological study.

HBV marker assays. The radioimmunoassay kits for 3 markers, i.e., AUSTRIA - II-125 for HBsAg, AUSAB - for Anti-HBs, and ANTI HBc RIAKIT - for Anti-

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¹Tohoku Rosai Hospital, Sendai, Japan. ²Institute of Occupational Medicine, Chinese Academy of Preventive Medicine, Beijing, China. ³Miyagi University of Education, Sendai, Japan. ⁴Osaka Occupational Health Service Center, Osaka, Japan.

⁵Department of Public Health, Shandong Medical University, Jinan, Shandong, China. ⁶Department of Public Health, Kyoto University Faculty of Medicine, Kyoto, Japan.

Address for correspondence: Masayuki Ikeda, Department of Public Health, Kyoto University Faculty of Medicine, Yoshida-konohe-cho Sakyo-ku, Kyoto 606-01, Japan.

HBc, were supplied by Abbott Laboratories (North Chicago, IL, U.S.A.). The cut-off indices for the identification of positive cases (to be abbreviated as HBsAg⁺, Anti-HBs⁺, and anti-HBc⁺) were set at >5, >2, and >70%, respectively.

Statistical evaluation. Statistical significance of difference in prevalence was evaluated by means of chi-

square test.

RESULTS

Prevalence of the 3 HBV infection markers among the study population

The prevalence of cases positive to the three markers are summarized in Tables 1 and 2. Those positive to

Table 1. Prevalence of hepatitis B virus (HBV) infection markers among factory workers in Yantai.

HBV infection marker			Number of cases		
HBsAg	Anti-HBs	Anti-HBc	Men	Women	Sum
-	-	-	64 (26.3)	62 (33.9)	126 (29.6)
-	+	-	12 (4.9)	4 (2.2)	16 (3.8)
-	-	+	25 (10.3)	14 (7.7)	39 (9.2)
-	+	+	79 (32.5)	58 (31.7)	137 (32.2)
+	-	-	27 (11.1)	24 (13.1)	51 (21.0)
+	+	-	0 (0.0)	0 (0.0)	0 (0.0)
+	-	+	33 (13.6)	19 (10.4)	52 (12.2)
+	+	+	3 (1.2)	2 (1.1)	5 (1.2)

In total, 426 adults (243 men and 183 women) were studied. The numbers in the table are the numbers of cases and the percentages in parentheses. + : Positive. - : Negative.

Table 2. Prevalence of HBsAg⁺, anti-HBs⁺ and anti-HBc⁺ cases by age and by sex.

Sex	Age range (years)	No. of sera tested	Indicative of HBV infection				HBV marker negative ^c
			HBsAg ^a	Anti-HBs ^a	Anti-HBc ^a	Anti-HBs ^a or Anti-HBc ^{a,b}	
Men							
	15-19	16	3 (18.8)	6 (37.5)	9 (56.3)	9 (56.3)	6 (37.5)
	20-29	168	51 (30.4)	50 (29.8)	92 (54.8)	96 (57.1)	51 (30.4)
	30-39	34	5 (14.7)	21 (52.9)	18 (52.9)	24 (70.6)	6 (17.6)
	40-49	18	2 (11.1)	14 (77.8)	16 (88.9)	18(100.0)	0 (00.0)
	≥ 50	7	2 (28.6)	3 (42.9)	5 (71.4)	5 (71.4)	1 (14.3)
	Total	243	63 (25.9)	94 (38.7)	140 (57.6)	152 (62.6)	64 (26.3)
Women							
	15-19	22	7 (31.8)	6 (27.3)	7 (31.8)	8 (36.4)	9 (40.9)
	20-29	86	24 (27.9)	27 (31.4)	38 (44.2)	40 (46.5)	32 (37.2)
	30-39	37	8 (21.6)	15 (40.5)	21 (56.8)	21 (56.8)	12 (32.4)
	40-49	24	4 (16.7)	9 (37.5)	16 (66.7)	17 (70.8)	6 (25.0)
	≥ 50	14	2 (14.3)	7 (50.0)	11 (78.6)	11 (78.6)	3 (21.4)
	Total	183	45 (24.6)	64 (35.0)	93 (50.8)	97 (53.0)	62 (33.9)
Men and women combined							
	15-19	38	10 (26.3)	12 (31.6)	16 (42.1)	17 (44.7)	15 (39.5)
	20-29	254	75 (29.5)	77 (27.6)	130 (51.2)	136 (53.5)	83 (32.7)
	30-39	71	13 (18.3)	36 (50.7)	39 (54.9)	45 (63.9)	18 (25.4)
	40-49	42	6 (14.3)	23 (54.8)	32 (76.2)	35 (83.3)	6 (14.3)
	≥ 50	21	4 (19.0)	10 (47.6)	16 (76.2)	16 (76.2)	4 (19.0)
	Total	426	108 (25.4)	158 (37.1)	233 (54.7)	249 (58.5)	126 (29.6)

The values in the table are the number of cases and the percentages in parentheses.

+ : Positive. ^a Positive to either anti-HBs or anti-HBc. ^b Over-all rate of infection as defined by the rate of these positive to any of the 3 markers. ^c Negative to all of the 3 markers tested.

HBsAg accounted for one fourth of the population studied with no significant difference in the prevalence between the two sexes ($p > 0.10$), and about a half of the HBsAg+ people were negative to the 2 antibody items. In contrast, about one third of the people studied were anti-HBs+ and anti-HBc+ in both sexes, and somewhat less than one third was negative to all of the 3 infection markers (Table 1). Thus, well over two thirds of the study population were either currently or previously infected with HBV.

Very few (1%) were positive to all the three markers, as theoretically expected. In such cases, they were very weakly anti-HBs+ with titers just above the cut-off point, whereas anti-HBc titers were high and HBsAg titers were various depending on the cases.

Age-dependent changes in HBV infection rates

The observed cases were further classified by sex and by decade of years of ages of the subjects (Table 2). There is a gradual age-dependent decrease in HBsAg+ prevalence both in men and women, albeit the rate for those at the ages of 19 years or less (18.8% for men and 31.8% for women) may be comparable to that for 20s; no significant difference in the prevalence was detected between those at less than 20 years of age and those at 20-29 years, when the two sexes were combined ($p > 0.10$). A high rate of 28.6% for >50 year-old men should be considered not reliable because only 7 subjects were examined.

Both anti-HBs+ and anti-HBc+ rates gradually increased in parallel in both sexes as ages advanced, so that about 80% or more of the population acquired immunity to HBV infection at the age of 40 years (i.e., either anti-HBs+ or anti-HBc+, or anti HBs+ and anti-HBc+). When positive reaction in any of the three infection markers (i.e., HBsAg+, anti-HBs+ or anti-HBc+) were considered to be indicative of past or current HBV infection, almost all subjects (more than 85%) had experienced HBV infection before the age of 50, whereas less than 15% of the people remained negative to any of the three HBV infection markers at this stage of life.

DISCUSSION

The present study of a Yantai population has shown that the rate of those positive to HBsAg was as high as 25.4% (25.9% in men and 24.6% in women), and that the rate when two sexes were combined was highest (i.e., 29.5%) at the ages of 20s followed by gradual decrease at higher ages (about 20% or less). The overall HBV infection rate as calculated by those positive to any of the three markers studied was 70.4%.

A growing number of papers have been published in

recent years to report the prevalence of HBV infection especially in terms of HBsAg+, and in some cases as the positivities to the three infection markers, in various cities and provinces in China^{5-7,11-18,20-40}. The results of the reviewing are summarized in Table 3. In comparative evaluation of the results in which radioimmunoassay, hemagglutination assay or the both in combination were employed, it should be taken into account that the sensitivity of the two methods vary and that hemagglutination method employed was reported to be less sensitive than the radioimmunoassay^{12,37}. Nevertheless, it is conceivable from the table that the HBsAg+ rate for the present Shandong examinees, 25.4%, is markedly higher than the values reported for various provinces including Guangxi Province where PHC mortality is known to be very high especially in men⁴¹; the values higher than the present observation are usually associated with known HBV infection²⁸ or inclusion of hepatitis cases³⁸.

The anti-HBs+ and anti-HBc+ rates were not remarkably high so that the over-all rate of HBV infection of the present study population is only comparable to the values for other provinces. It was previously pointed out that the prevalence of HBV infection is lower in a large city like Beijing (although not in Shanghai where PHC mortality is reported to be high⁴¹) than in rural provinces¹⁷. Simple urban-rural difference, however, will not be sufficient to explain rather unusually high HBsAg rate among the working population in the present study (Tables 1 and 3).

For comparison with the present observation, 6 reports²⁸⁻³⁵ are available in addition to an early report of Beasley and his co-workers³¹ on HBV infection in Shandong Province in particular. The reported HBV infection prevalence as defined by positive to any of the 3 markers reported in recent studies²⁸⁻³⁵ are in a wide range of 27.4%³⁴ to 78.3%³⁵. Nevertheless, the prevalence of HBsAg+ cases are all well below 10%.

Beasley et al.³¹ found that the HBsAg+ prevalence among former Shandong Province residents currently in Taiwan were 9.3%, the value being not higher as compared with the values for those from northern China (11.2% on an average) and probably lower than the values for those from southern China (17.7%). In agreement with rather low HBsAg+ prevalence, the rates of mortality from liver cancer (per 10⁵ population, based on deaths in 1973 to 1975, and age-adjusted to 1964 census population of China⁴¹) was 11.57 for men (4.24 for women) in Shandong Province; the values are not higher than the values for the whole country (14.52 for men and 5.61 for women), and quite lower than those for Guangxi Province (26.55 for men and 6.63 for women) where HBV infection prevalence

Table 3. Comparison of HBV infection marker prevalence in Chinese populations.

Study area ^a	Population		Assay by R or H ^b	HBV infection marker positive (%)				Reference
	No.	Notes		HBsAg	Anti-HBs	Anti-HBc	Over-all ^c	
Anhui	503	Factory workers	R	8	46	— ^d	53	16
Beijing	398	All ages	R	7	—	—	—	20
<i>ibid.</i>	600	Dental workers	H	6	20	—	26	21
<i>ibid.</i>	491	All ages	R	7	37	46	52	22
<i>ibid.</i>	968	Factory workers	R	4	37	38	44	17
Fujian	407	Children (1979) ^e	H	17	—	—	—	23
<i>ibid.</i>	6558	Children (1987) ^f	H	7	—	—	—	23
Guandong	265	Controls to PHC	H	7	—	—	—	5
<i>ibid.</i>	2443	Male prisoners	R	25	46	20	81	24
Guangxi	173	Controls to PHC	H	16	12	—	—	13
<i>ibid.</i>	1310	Adults	H	15	9	35	—	12
<i>ibid.</i>	35041	All ages	H	13	8	—	—	11
<i>ibid.</i>	49	Controls to PHC	R	11	63	57	88	6
<i>ibid.</i>	49	Controls to PHC	R	23	63	57	88	15
<i>ibid.</i>	11072	Adults	H	17	—	—	—	7
<i>ibid.</i>	304	Adults men	R	22	—	—	—	14
Henan	1064	All ages	R	—	26	—	—	25
<i>ibid.</i>	579	Farmers ^g	R	32	38	60	79	26
Hunan	3089	All ages	R&H	18	32	74	81	27
Jiangsu	290	Factory workers	R	9	53	63	72	18
Liaoning	66	Factory workers	R	8	39	35	48	18
Shandong	926	Various	R	5	—	—	—	28
<i>ibid.</i>	1367	All inhabitants	H	7	—	—	—	29
<i>ibid.</i>	436	All inhabitants	H	6	10	40	47	30
<i>ibid.</i>	107	Controls to PHC	H	8	55	22	58	31
<i>ibid.</i>	977	Farmers	H	9	19	7	27	32
<i>ibid.</i>	401	Clinical staff	R	7	41	68	78	33
<i>ibid.</i>	426	Factory workers	R	25	37	55	70	Present study
Shanghai	4822	Adults	H	10	9	—	—	34
<i>ibid.</i>	365	All ages	R	7	37	48	57	35
<i>ibid.</i>	520	Preschool children	R	8	—	—	22	36
<i>ibid.</i>	290		R	8	48	55	65	18
Shanxi	521	All ages	R&H	8	23	19	39	37
<i>ibid.</i>	2122	All ages ^h	R	36	31	62	78	38
<i>ibid.</i>	429	Factory workers	R	8	40	49	56	18
Sichuan	423	Adult blood donors	H	4	85	—	—	39
Zhejiang	5168	All ages	H	13	—	—	—	40

^a Name of province, except for two cities of Beijing and Shanghai. ^b R for radioimmunoassay, and H for hemagglutination assay. ^c Over-all rate of infection as defined by the rate of those positive to any of the 3 markers. ^d Not studied. ^e 1-10 year-old children, studied in 1979. ^f 1-6 year-old children, studied in 1987. ^g Highly infected with HBV. ^h 316 hepatitis cases are included.

is also high (Table 3). Thus, it could be the case that the HBV infection prevalence is specifically high in the present study population, even though the prevalence may be generally low in Shandong Province; such may be quite probable bearing in mind that Shandong Province has a large population of 80 millions in a large area of 150,000 km².

The age-dependent changes in HBsAg⁺ prevalence of the present study population in Yantai is depicted in

comparison with the counterpart observation in Beijing, Shanghai, Wuxi, Xian and Hefei made by the present study group¹²⁻¹⁸ in Figure 1; a high prevalence (33%) observed in less than 20 year-old subjects in Wuxi may be due to the fact that only a small number of people (15 subjects) were examined in this age group, and therefore not depicted in the figure. It is apparent from Figure 1 that the prevalence in Yantai subjects up to 49 years of age is much higher than their

Table 4. HBsAg⁺ prevalence in Shandong Province by ages.

Study Region	No. of subjects	Age range							Reference
		0 to 9	10 to 19	20 to 29	30 to 39	40 to 49	50 & over	All ages	
Changxue County	926	3.2	3.4	4.3	6.0	10.5	6.6	5.4	27
Huimin County	1367	4.5	6.4	12.2	8.0	11.8	1.8	6.5	28
Jinan City	436	0.0	4.4	6.9	6.0	12.2	10.6	6.2	29
Shandong Province ^a	107							8.4	30
Penglai County ^a	977							8.6	31
Zibo City ^a	401							7.2	32
Yantai City	426	— ^c	26.3	29.5	18.3	14.3	19.0	25.4 ^a	Present study

^a Significantly different from counterpart values ($p < 0.01$).^b Break-down by age is not given. ^c Hospital patients from the Province. ^d Not studied.

counterparts in other cities, indicating that HBV infection is endemic among this study population. In addition, the fact that the persistent carrier rate is almost 1.5-fold higher in younger people (those below

30 years of age) as compared with older people suggest that an unidentified episode might have happened in recent 10-20 years which provoked the increase in the HBV carrier rate. It would be more informative if the rates for younger inhabitants were available.

Several factors have been discussed in explaining the high HBsAg prevalence among various Chinese populations studied. For example, Luo et al.¹⁵ considered both vertical transmission from carrier mothers to their new-born babies and close family contacts during the post-natal period as routes of HBV infection to produce persistent HBsAg carriers. Tang et al.¹² examined HBV infection markers of 35 fetuses from HBsAg⁺ mothers after induced abortion in comparison with 10 fetuses from HBsAg⁻ mothers, and observed that the sign of HBV infection was positive in sera of 7 cases in the former group (20%) in contrast to none in the latter. In the former group, 12 cases out of 27 liver tissues (44.4%) were positive to the infection when P-labeled HBV-DNA was employed as a probe, suggesting that intra-uterine infection is also an important mode of HBV transmission¹². In this connection, it is worthy to note that Duan et al.¹³ in fact succeeded to interrupt mother-to-baby transmission of HBV by the administration of HBV vaccine to the babies born to HBsAg⁺ mothers. Regarding the latter possibility, Huan et al.¹⁶ observed in their epidemiological study of preschool children in Shanghai that the habit of pre-mastication of food to feed children is associated with two-fold higher risk of the infection within a family. Opinions are equivocal among Chinese scientists on possible contribution of aflatoxin B contamination of food as a co-causative factor of PHC in combination with persistent HBV infection, in explaining high PHC incidence among Guangxi inhabitants^{13,14}.

A few more reports are available in which trials were made to explain the mode of HBV infection among Chinese inhabitants outside the Continent. In Sin-

Figure 1. Age-dependent changes in HBsAg⁺ rate among people in Yantai in comparison with those in other cities. Rates for two sexes in combination are shown. The values for cities other than Yantai are cited from Seiji et al.¹⁶⁻¹⁸. Symbols are: open squares for Yantai, solid squares for Beijing, open triangles for Shanghai, solid triangles for Wuxi, open circles for Xian, and solid circles for Hefei.

gapore. Quak et al.⁴⁴ examined Chinese children for HBV infection in comparison with their counterparts of Malay and Indian origin and found that, although HBsAg⁺ prevalence appeared to be almost comparable among the 3 ethnic groups, the prevalence of anti-HBs⁺ and anti-HBc⁺ cases were significantly higher among Chinese children than in Malay or Indian children. In a study of babies born to HBsAg⁺ mothers in Taiwan, Stevens and others⁴⁵ observed that the risk of babies to be HBsAg⁺ increased when his/her mother had high titer HbsAg, when the umbilical cord blood was HbsAg⁺, or when his/her sibling was HbsAg⁺, and concluded that the vertical transmission occur rather frequently. In contrast, Lam et al.⁴⁶ observed a sharp increase in HBsAg⁺ prevalence from first (less than 10%) toward fourth decade (over 40%) of life (and then decrease thereafter) among Chinese population in Hongkong, and thought that the dominant mode of HBV transmission among Chinese people there was likely to be horizontal rather than vertical.

At the moment, no plausible explanation is available to understand the unusually high HBV infection prevalence among the population studied. Whether the prevalence is high in Yantai City in general or it is so among the study population only is still yet to be elucidated. Careful observation of the local culture and the way of daily life appears to be extremely important in order to identify the social habits which enhance the risk of infection at an early stage of life.

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