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A comparative study on serologic profiles of virus hepatitis B

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INTRODUCTION

Hepatitis B viral infection, one of the most-prevalent liver disorders in China and Korea, is a serious infectious disease as it has the potential of progressing into liver cirrhosis and primary hepatic carcinoma. China and Korea both belong to high-risk endemic regions of viral hepatitis[1]. The HBsAg positive rates in China ranged from 6.9%-17.9% by age, race and test methods[2-5]. In Korea, they were 6.5%-13.3% in all age groups[6-9], and 3.9%-5.9% in childhood groups[10-11]. There have been few comparative studies on Korean-Chinese and other Chinese. Considering the high mortality rates of liver cirrhosis or hepatoma among Korean-Chinese, HBsAg positive rate of Korean-Chinese must be higher than that of other Chinese. The positive rates of Korean-Chinese in Yanji and Longjing cities of Yanbian area by RPHA method were 7.5% and 7.1% respectively, which were higher than 6.2% and 4.7% in Han-Chinese respectively[12].

In regard to the possible reasons of such differences, some studies have laid special emphasis on social, economic and demographic variables such as age, sex, life style, and environment.

This study was conducted in order to assess the pattern of hepatitis B infection prevailing among Han-Chinese, Korean-Chinese, and Koreans. For collection of data, two serological surveys were carried out in 1996 in Korea and China respectively.

MATERIALS AND METHODS

Study areas

Study areas were Yangpyung County of Kyonggi Province in Korea and Helong County of Yanbian, a Korean Autonomous Prefecture in China. In Helong County, the proportion of residents by ethnicity were 55% for Korean-Chinese and 44% for Han-Chinese[13]. To compare the prevalence of hepatitis B between Korea and China, we carefully considered the characteristics of selected areas. In both areas, 70% of the residents were farmers. But the pattern of age distribution was different; the majority residing in Yangpyung County in Korea were more than 50 years old, while those in Helong County in China were over 40 years old.

Study subjects

Study subjects among ethnic groups were 556 Korean (male 41.7%, female 58.3%, $P<0.05$), 541 Korean-Chinese (male 51.6%, female 48.4%) and 261 Han-Chinese (male 39.5%, female 60.5%, $P<0.05$). These distributions by gender were statistically significant in Korean and Han-Chinese. Age distributions by ethnic groups were also significantly different; and the Koreans had older age and the Chinese had younger age. Age distributions by gender were not different between Korean and Korean-Chinese, but they were significantly different in Han-Chinese (Table 1). Therefore, this study showed the results with age-adjusted rates by gender.

Table 1 Characteristics of subject by ethnic groups[d]

Ethnic groups	Age (years)	Gender		Total
		Male	Female	
Korean-Chinese[b,c]	20-39	103	117	220
	40-49	89	77	166
	50-	87	68	155
Total		279	262	541
Han-Chinese[a,b,c]	20-39	42	103	145
	40-49	30	44	74
	50-	26	16	42
Total		98	163	261
Koreans[a,b]	20-39	43	70	113
	40-49	37	60	97
	50-	152	194	346
Total		232	324	556

[a]$P<0.05$ between sex, by χ^2 test; [b]$P<0.05$ among age groups, by χ^2 test; [c]$P<0.05$ among age groups by sex, by χ^2 test;
[d]Koreans-Chinese: Koreans in Yanbian in China, Han-Chinese: Chinese in Yanbian in China, Koreans: Koreans in Yangpyung in Korea.

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Questionnaires

The questionnaire survey gave direct interviews, including the relative factors on hepatitis B infection such as demographic characteristics, life style, vaccination and disease history.

Serologic tests

Serological markers on hepatitis B virus (HBsAg, anti-HBs and anti-HBc) were tested by EIA (enzyme immunoassays). Sera were stored in a deep freezer, at -30℃ until this test. The serologic tests were all done in Korea.

Statistical analysis

For comparison by ethnic groups, age-adjusted rates by direct method were used. The statistical significance was determined using χ^2 test or Mantel-Haenszel's χ^2-test on SPSS or EPISTAT.

RESULTS

There were no vaccinees on hepatitis B among Chinese, but the vaccination rate among Koreans was 32.4% (36.5% for males and 29.0% for females). The vaccination rate was 44.2% for the age group of 20-39 years, 45.4% for the age group of 40-49 years, and 24. 4% among those aged 50 and over (Table 2). In order to compare hepatitis B virus markers among ethnic groups, the vaccinees were excluded.

HBsAg positive rate of males was higher than that of females in the three ethnic groups. Age-adjusted HBsAg positive rates were 7.2%, 12.0% and 4.1% in Han-Chinese, Korean-Chinese, and Korean respectively (P<0.05). This order was same in both genders. But, the difference was statistically significant only in males (P<0.05). Anti-HBs positive rates of males were higher than those of females in Korean-Chinese and Korean, but the differences were not statistically significant. There was also no difference by gender in the Han-Chinese. The age-adjusted anti-HBs positive rate of Korean (62.5%) was the highest, of Korean-Chinese was 57.6%, and of Han-Chinese 49.2%. This order was true in males and females, but the differences among the three ethnic groups were not significant. Anti-HBc positive rates of males were higher than those of females in all three groups, but these differences were not significant. Age-adjusted anti-HBc positive rate was 69.7%, the highest in Korean-Chinese, 60.9% in Korean and 54.0% in Han-Chinese. This order was also found by gender, and these differences were all statistically significant (P<0.05).

The definition of hepatitis B infection was determined as cases that have any hepatitis B virus markers among HBsAg, anti-HBs and anti-HBc. The infection rate was higher in males than in females among the three ethnic groups. But the difference was significant only in Koreans (P<0.05). Age-adjusted infection rates were 78.6% in Korean, 77.0% in Korean-Chinese and 60.7% in Han-Chinese. These differences among the three ethnic groups were significant (P<0.05) in males, females and the total.

In Koreans, the HBsAg positive rate was lower than that of Korean-Chinese, but the HBV infection rate was not different from Korean-Chinese, and was higher than that of the Han-Chinese. In Korean-Chinese, the HBsAg positive rate and HBV infection rate were higher than those of the Han-Chinese. In the Han-Chinese, the HBV infection rate was the lowest and the percentage of those who are susceptible was the highest (Table 3).

We classified the serologic profiles into 8 types by 3 HBV markers, which are HBsAg, anti-HBc and anti-HBs. Mushahwar *et al* (1981)[21] used 15 classifications by 5 HBV markers including HBeAg and anti-HBe, to determine the HBV infectivity. We used 8 types for the description of HBV serologic profiles in the cross-sectional study. Type I of our classification means those susceptible who have all three negative markers. These percentages of those susceptibles were higher in females than in males in all three ethnic groups. The percentage was 18.6% for Koreans or Korean-Chinese, and 36.7% for Han-Chinese. In females, the percentage was 40.5% for Han-Chinese, 29.6% for Korean, and 23.7% for Korean-Chinese. Among HBsAg positive serologic profiles, type VII was dominant. But, varied types such as V, VI and VIII were found only in Korean-Chinese and Han-Chinese excluding Koreans. Koreans had only one type VII, among HBsAg positive profiles. The percentage of HBsAg negative combination (HBsAg- and anti-HBs+ and/or anti-HBc+), were 78.5% and 65.5% for Korean, 67.5% and 67.6% for Korean-Chinese and 53.1% and 52.1% for Han-Chinese. Among these profiles, type IV was dominant in all three ethnic groups (Table 4).

Table 2 Rate of vaccination by sex and age in Koreans[b]

Age (yrs)	Male[a]			Female[a]			Total		
	No. of respondents	No. of vaccinces	%	No. of respondents	No. of vaccinces	%	No. of respondents	No. of vaccinces	%
20-39	43	19	44.2	70	31	44.3	113	50	44.2
40-49	37	23	62.2	60	21	35.0	97	44	45.4
50-	152	44	28.9	194	42	21.6	346	86	24.9
Total	232	86	37.1	324	94	29.0	556	180	32.4

[a]P<0.05 among age groups, by χ^2 test; bKoreans: Koreans in Yangpung in Korea.

Table 3 Positive rates and infection rate of Hepatitis B virus by sex and ethnic groups[e]

	Male			Female			Total		
	No. of tested	Crude rate(%)	Age-adjusted rate[d](%)	No. of tested	Crude rate(%)	Age-adjusted rate[d](%)	No. of tested	Crude rate(%)	A ge-adjusted rate[d](%)
HBsAg positive rate[a,c]									
Korean-Chinese	279	14.0	14.8	262	8.8	8.8	541	11.5	12.0
Han-Chinese	98	10.2	9.4	163	7.4	6.0	261	8.4	7.2
Korean	146	2.7	6.1	230	4.8	3.0	376	4.0	4.1
Anti-HBc positive rate[a,b,c]									
Korean-Chinese	279	74.6	73.2	262	68.3	66.0	541	71.5	69.7
Han-Chinese	98	58.2	59.1	163	50.9	50.4	261	53.6	54.0
Korean	140	69.3	61.3	226	58.0	60.0	366	62.3	60.9
Anti-HBc positive rate									
Korean-Chinese	279	62.4	61.1	262	56.5	54.0	541	59.5	57.6
Han-Chinese	98	46.9	48.4	163	49.1	51.7	261	48.3	49.2
Korean	146	62.3	69.1	230	55.7	58.6	376	58.2	62.5
HBV infection rate[a,b,c]									
Korean	140	81.4	85.3	226	70.4	74.0	366	74.6	78.6
Korean-Chinese	279	81.4	79.7	262	76.3	74.1	541	78.9	77.0
Han-Chinese	98	63.3	63.4	163	59.5	59.8	261	60.9	60.7

[a]$P<0.05$ among 3 ethnic groups in male, by χ^2 test; [b]$P<0.05$ among 3 ethnic groups in female, by χ^2 test; [c]$P<0.05$ among 3 ethnic groups in total, by χ^2 test; [d]Age-standardized rates (standard population; Helong in 1997 and Yangpyung in 1995); [e]Korean-Chinese: Koreans in Yanbian in China, Han-Chinese: Chinese in Yanbian in China, Koreans: Koreans in Yangpyung in Korea.

Table 4 Serological profiles of hepatitis B virus markers by sex and ethnic groups[a]

Gender ethnic groups	Serological profiles* (%)								Total
	I	II	III	IV	V	VI	VII	VIII	
HBsAg	-	-	-	-	+	+	+	+	
Anti-HBc	-	-	+	+	-	-	+	+	
Anti-HBs	-	+	-	+	-	+	-	+	
Male Korean-Chinese	52(18.6)	16(5.8)	27(9.7)	145(52.0)	1(0.4)	2(0.7)	25(9.0)	11(3.9)	279(100.0)
Han-Chinese	36(36.7)	3(3.1)	8(8.2)	41(41.8)	2(2.0)	0(0.0)	6(6.1)	2(2.0)	98(100.0)
Koreans	26(18.6)	17(12.1)	22(15.7)	71(50.7)			4(2.9)		140(100.0)
Female Korean-Chinese	62(23.7)	17(6.5)	35(13.4)	125(47.7)	3(1.1)	1(0.4)	14(5.3)	5(1.9)	262(100.0)
Han-Chinese	66(40.5)	9(5.5)	8(4.9)	68(41.7)	4(2.5)	1(0.6)	5(3.1)	2(1.2)	163(100.0)
Koreans	67(29.6)	28(12.4)	21(9.3)	99(43.8)			11(4.9)		226(100.0)

[a]Korean-Chinese: Koreans in Yanbian in China, Han-Chinese: Chinese in Yanbian in China, Koreans: Koreans in Yangpung in Korea.

DISCUSSION

Since 1980, China has produced hepatitis B vaccines and by regulations, children must be vaccinated. However, vaccination against HBV was not mandatory in adults. Therefore, none of study subjects in China were vaccinated, while in Korea, 32.4% were vaccinated. It implies that the circumstances of HBV infection and transmission were different between China and Korea. Age-adjusted HBsAg positive rate of Korean-Chinese was 12.0%, higher than the 10% previously reported in China as a whole[14]. Moreover, the rate was higher than the 8.0% for the Korean-Chinese in Yanbian area during the 1980s[12]. The rate for Han-Chinese (7.2%) was less than the national level (10%) in China, and the same or less than that of other reports[2-5]. However, no other reports were found from Yanbian area, the differences did not reflect the chronological change. In Koreans, the rate for non-vaccinees was 4.1%, which was less than other reports (6.5%-13.3%)[6-10,15,16].

Korean and Korean-Chinese are the same race, but HBsAg positive rates were different and increased with time for Korean-Chinese and decreased with time for Koreans. The difference between Korean and Korean-Chinese seems to be caused mostly by vaccination. Other factors such as socioeconomic status, sanitary status and medical support appear to influence HBV infection and transmission[6,7,11,17]. The difference between Korean-Chinese and Han-Chinese resulted from cultural difference such as life style, food habits and susceptibility[6,7,11,17]. The rate for Korean-Chinese was more similar to the Han-Chinese than to Koreans, which suggests that environmental factors are more important than genetic factors on HBV.

Positive anti-HBc is difficult to determine definitely. Type IV (anti-HBs+, anti-HBc+, and HBsAg-) and VIII (anti-HBs+ anti-HBc+, and HBsAg+) are in recovery phases caused by the positive anti-HBs. But type III (anti-HBs-, anti-HBc+, and HBsAg-) and VII (anti-HBs- anti-HBc+, and HBsAg+) mean acute or chronic infection. The order of high anti-HBc positive rates among the three ethnic groups was Korean-Chinese, Korean and Han-Chinese. This order was too

difficult to interpret like the anti-HBc.

Positive anti-HBs means having immunity against HBV. Age-adjusted anti-HBs positive rate for Chinese (57.6% for Korean-Chinese and 49.2% for Han-Chinese) was higher than that of other reports[2-5], however, in Korean (the 62.5%) it was higher[8,18] or lower than that of other reports[7,19]. Even though the difference among the three ethnic groups was not statistically significant, the reason why the anti-HBs positive rate for Korean (62.5%) was the highest, can be explained by the different serological profiles. Among the anti-HBs positive Koreans, 20.9% was type II (anti-HBs+, anti-HBc-, and HBsAg-), which indicates remote past infection, but, 10.3% and 9.5% among Korean-Chinese and Han-Chinese. Other types like IV (anti-HBs+, anti-HBc+, and HBsAg-), VI (anti-HBs+, anti-HBc-, and HBsAg+) and VIII (anti-HBs+, anti-HBc+, and HBsAg+) indicate the recovery phase of acute infection as a whole (IV, recovery phase of HBV infection; VI, unknown; and VIII, circulating immune complex of HBsAg or reinfection with different HBsAg subtype or process of seroconversion from HBsAg to anti-HBs). Therefore, positive anti-HBs Koreans had more remote infections than Korean-Chinese and Han-Chinese, which could be also applied to the exploration of HBV infection rates. HBV infection was determined by having had any one of the positive HBV markers among HBsAg, anti-HBs and anti-HBc. The order of high HBV infection rates among the three ethnic groups was the same as anti-HBs, Korean, Korean-Chinese and Han-Chinese. The difference was statistically significant ($P<0.05$).

HBV infection rates in Korean-Chinese were 81.4% in males and 76.3% in females, which were 80.8% in males of Hunan area and 75.5% in female of Guangxi of China[5]. The rates for Koreans were 81.4% in males and 70.4% in females. Therefore, even if the HBsAg rates have been decreasing as compared with that of the 1980s, HBV infection rate did not drop. According to Maynard *et al*[20]. 70%-90% of the population were infected with HBV in the highly endemic areas. Hence, Korea and Yanbian were included in the endemic area.

The fact that HBV infection rates for Korean-Chinese and Koreans were higher than those of the Han-Chinese seems to be caused by susceptibility and cultural factors such as life style and dining habits. Ahn *et al*[19] reported the association between HBV infection and behavioral characteristics such as life style, dining habit and sanitary status. Therefore, to determine the reason for the higher rate of HBV in Koreans and Korean-Chinese, more studies dealing with genetic factors and behavioral factors are needed.

In regard to positive HBsAg rate, the results showed difference by ethnic groups in the same area. Consequently, for each of the areas and the ethnic groups, the HBV infection and transmission must be differentiated[21]. For the clarification of the natural course on HBV, more detailed immigration studies and follow-up efforts should also be made.

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