HEPATITIS B AND C VIRUS INFECTION AMONG ADULT WOMEN IN JILIN PROVINCE, CHINA : AN URBAN-RURAL COMPARISON IN PREVALENCE OF INFECTION MARKERS

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Abstract. Twin seroepidemiological surveys on prevalence of hepatitis B and C virus (HBV and HCV, respectively) infection were conducted on 100 adult women in total, 50 each in the provincial capital of Changchun and in a farming village in the vicinity in Jilin Province, northeast China. Positivity to three markers on HBV (*ie* HBsAg$^+$, anti-HBs$^+$, and anti-HBc$^+$) was examined by RIA methods, and to one on HCV (anti-HCV$^+$) by EIA. The results were evaluated in combination with two foregoing studies in Shandong and Shaanxi Provinces, and with special reference to possible urban-rural differences in prevalence. The prevalence of HBsAg$^+$ cases was rather low (*ie* 9% when two groups were combined), but that of anti-HBs$^+$ and anti-HBc$^+$ cases was high, being 50% and 45%, respectively. Thus, the rate of HBV$^+$ cases was 62%. The rate for HCV$^+$ cases was 3%. The comparison of the prevalence between the city group and the village group showed that the rates for anti-HBs$^+$ and HBV$^+$ were significantly or marginally higher in the former group than in the latter, respectively. The HCV$^+$ prevalence rate for the city group (4%) also tended to be higher than the corresponding rates for the village group (2%), although the difference was statistically insignificant. When evaluated together with the observation in Shandong and Shaanxi Provinces, it appears possible to generalize that the HBV infection prevalence is not higher and probably lower in rural areas than in urban areas, and that such may also be the case for the HCV infection prevalence.

INTRODUCTION

It is generally accepted that high prevalence of infection to hepatitis B virus (HBV) and hepatitis C virus (HCV) infection early in life is associated with increased incidence of hepatocellular carcinoma (HCC) in the later stage of life (International Agency for Research on Cancer, 1994). The knowledge that the prevalence, especially that of HBV, is high in continental China (International Agency for Research on Cancer, 1994; Yao, 1996) has been attracting attention of seroepidemiologists, hepatologists and public health scientists both in and outside of the country (Liu *et al*, 1991; Tao *et al*, 1991, 1992; Qin *et al*, 1992; Yuki *et al*, 1992; Li *et al*, 1993, Li *et al,* 1998; Okuno *et al*, 1994; Ye *et al*, 1994; Deng *et al*, 1995; Di Bisceglie, 1995; Mansell and Locarnini, 1995; Qi and Wang, 1995; Di, 1996; Hao *et al*, 1996; Shi and Bian, 1996; Zhou *et al*, 1996; Liu *et al*, 1997; Cao *et al*, 1998; Huang *et al*, 1998; Zhang *et al*, 1998; Cui *et al*, 1999) including this group (Seiji *et al*, 1991a,b,c; Shimbo *et al*, 1997, 1998).

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Because blood sampling is essential in seroepidemiological studies, survey sites inevitably tend to be biased to urban areas; in cities, less people hesitate to accept venipuncture, and transport as well as medical facilities are more readily available. A majority of people in China, however, live in rural areas, and the living standard when evaluated in terms of monetary income is reported to be lower in villages than in cities (Ge *et al*, 1996).

Bearing this difference in mind, this study group has conducted two surveys on HBV and

HCV infection prevalence in farming areas in parallel with the provincial capitals, *ie* one case was twin surveys in Shandong Province in central China (Shimbo *et al*, 1997) and the other was triplet surveys in Shaanxi Province in northwest China (Shimbo *et al*, 1998). In addition, new twin surveys were completed recently in Jilin Province in northeast China. The study results in Jilin province will be described in this paper in combination with the results of the two foregoing studies (Shimbo *et al*, 1997, 1998). Efforts are focused to examine possible urban-rural differences in HBV and HCV infection prevalence.

MATERIALS AND METHODS

Study population and study design

An urban-rural comparison survey was conducted in September, 1999 in the city of Changchun, the provincial capital, and in a farming village in Dehui county (to be called Dehui) in Jilin Province, northeast China; the village is some 100 km NNE of Changchun. In each survey site, 50 adult nonsmoking and non-habitually drinking healthy adult women volunteered to participate in the survey; none had a history of blood transfusion, and subjects clinically ill at the time of the survey or with systemic diseases in past were excluded. Changchun participants (25 to 58 years of age; the city group) were staff of a public health institution, whereas those from the village were farmers (21 to 61 years; the village group) producing primarily rice and maize. The villagers depend on well water for daily life. The participants were all married except for five people in the city group and one in the village group. Blood samples were drawn from the cubital vein shortly (0.5 to 1 hour) after lunch in case of the city group, and 2 to 3 hours after breakfast in case of the villagers.

Assay for HBV and HCV infection markers, and liver function tests

Serum samples were obtained by on-site centrifugation for separation, kept chilled, and transferred to two clinical laboratories for analyses. HBV and HCV infection markers were assayed in a laboratory in Japan by commercial RIA or EIA kits; HBV surface antigen (HBsAg) by AUSRIA® II-125, HBV surface antibody (anti-HBs) by AUSAB®, HBV core antibody (anti-HBc) by RIA KIT®, HCV antibody (anti-HCV) by HCV EIA II (all from Abbott-Dianabot, Tokyo, Japan). The cut-off point for negativity was <1 for HBsAg and anti-HBs (as a cut-off ratio), <30% for anti-HBc (as a suppression rate) and <1 for anti-HCV (as a cut-off index). A subject was considered HBV^+ when positive to any of the HBV infection markers, and HBV^- when negative to all the three markers.

Serum biochemical studies were undertaken in a laboratory in China. They included AST (EC 2.6.1.1), ALT (EC 2.6.1.2), γ-GTP (EC 2.3.2.1), ALP (EC 3.1.3.1), LDH (EC 1.1.1.27), LAP (EC 3.4.1.1), CHE (EC 3.1.1.8), total protein, albumin, total cholesterol, HDL-cholesterol, triglyceride, creatinine, BUN, and uric acid, and was assayed with a conventional autoanalyzer (Hitachi Model 7150, Tokyo, Japan). Among them, the findings on AST, ALT and γ-GTP were taken in this study as liver function markers. The normal range for the assays in the laboratory was 6 to 37 IU/l for AST, 6 to 40 IU/l for ALT and 0 to 50 IU/l for γ-GTP.

Statistical analysis

Chi-square test was employed for detection of differences in prevalence.

RESULTS

Prevalence of HBV and HCV marker-positive cases

Prevalence of the subjects positive to HBs antigen ($HBsAg^+$), anti-HBs (anti-HBs^+), anti-HBc (anti-HBc^+), any of the three HBV infection markers (HBV^+), or anti-HCV (anti-HCV^+) is summarized in Table 1. The subjects were classified by the site of the study into the city group and the village group, and further classified by age (*ie* those at the age of 40 years or less, and those at or above the age of 41 years). The prevalence of $HBsAg^+$ cases was generally low (*ie* 5 to 13%), but that of anti-HBs^+ or anti-HBc^+ cases was as high as 30 to 63%, or 35 to 50%, respectively, depending on the age range and the marker studied. Thus, the whole age range rate of HBV^+ cases was 70% in the city group and 54% in the village group.

The point worthy of attention is the fact that the prevalence of $HBsAg^+$, anti-HBs^+, anti-HBc^+ and therefore HBV^+ cases tended to be higher in the city group than the village group, although the difference was statistically significant only for anti-HBs^+ ($p < 0.05$), barely so for HBV^+ ($0.05 < p < 0.10$),

Table 1
Prevalence of hepatitis B and C virus infection markers in the city and village groups.

Group and age range (years)	No. of cases (%)	Indicative of HBV infection				Anti-HCV⁺ (%)	HBV⁺ and anti-HCV⁺ (%)
		HBsAg⁺ (%)	Anti-HBs⁺ (%)	Anti-HBc⁺ (%)	HBV⁺ (%)		
City							
25-40	26	3 (12)	16 (16)[a]	12 (46)	19 (73)[b]	1 (4.0)	1 (4.0)
41-58	24	3 (13)	15 (63)	11 (46)	16 (67)	1 (4.0)	1 (4.0)
Total	50	6 (12)	31 (62)[a]	23 (46)	35 (70)[b]	2 (4.0)	2 (4.0)
Village							
21-40	20	1 (5)	6 (30)	7 (35)	9 (45)	1 (5.0)	1 (5.0)
41-61	30	2 (7)	13 (43)	15 (50)	18 (60)	0 (0)	0 (0)
Total	50	3 (6)	19 (38)	22 (44)	27 (54)	1 (2.0)	1 (2.0)
City + Village							
21-40	46	4 (9)	22 (48)	19 (41)	28 (61)	2 (4.0)	2 (4.0)
41-61	54	5 (9)	28 (52)	26 (48)	34 (63)	1 (2.0)	1 (2.0)
Total	100	9 (9)	50 (50)	45 (45)	62 (62)	3 (3.0)	3 (3.0)

HBsAg=HBV antigen; anti-HBs=HBV surface antibody; anti-HBc=HBV core antibody; anti-HCV= HCV antibody.

The values are the number of cases (% in parentheses). [a] and [b] show that the prevalence is significantly ($p < 0.05$) or marginally significantly ($0.05 < p < 0.10$) higher in the group with the mark than in the counterpart group. There is no significant ($p > 0.10$) difference in the prevalence of HBsAg⁺, anti-HBs⁺, anti-HBc⁺, anti-HCV⁺, or HBV⁺ and anti-HCV⁺ between two age groups, or among the two regional groups (the two age sub-groups combined).

and insignificant in cases of HBsAg⁺ and anti-HBc⁺ ($p > 0.10$ for both cases). The tendency was most remarkable when the prevalence among younger subjects were compared, *eg* the anti-HBs⁺ prevalence among 25-40 year-old women was 61% in the city group in contrast to the prevalence of 30% in the village group ($p < 0.05$).

With regard to HCV infection prevalence, age-dependent difference in the prevalence rate was not evident either in the city group and in the village group. Regarding the cases of double infection to HBV and HCV (*ie* HBV⁺ and anti-HCV⁺), all of those positive to anti-HCV were also HBV⁺. Accordingly, the results were the same for the double infection cases as for anti-HCV⁺ cases.

No clear association was detected between HBV/HCV seropositivity and liver dysfunction. One possible exceptional case was a 35 year-old woman in the city group. She was anti-HBs⁺ and anti-HBc⁺ (but anti-HCV⁻), and had moderately high AST (34 IU/l), ALT (75 IU/l) and γ-GTP (61 IU/l). Her triglyceride (230 mg/100 ml; normal range, 44-151 mg/100 ml) and total cholesterol (236 mg/100 ml; normal range, 120-220 mg/100 ml) however were also elevated, suggesting that the elevation in the enzyme activities was probably due to fatty liver rather than direct effects of virus infection.

DISCUSSION

Table 2 summarizes the comparison of the present observations with the results in two previous studies by this study group (Shimbo *et al*, 1997, 1998) on urban-rural comparison. The whole age group is taken for comparison because age-dependent changes in the prevalence were statistically insignificant ($p > 0.10$; Table 1). It should be added that the age distribution was essentially the same in the three surveys. It should be noted in making comparison that radioimmunoassay (RIA) was employed throughout these studies (Shimbo *et al*, 1997, 1998), including the present one.

Comparison of urban and rural groups is given in Table 2. Statistical analysis showed that there was no significant ($p > 0.10$) difference between the city group and the village group in the prevalence of HBsAg⁺. The prevalence of anti-HBs⁺ was higher ($p < 0.01$) in the city group than in the village group, whereas anti-HBc⁺ might be higher

Table 2
Prevalence of hepatitis B and C virus infection markers in the three provinces.

Group, province, age range (years)	No. of cases (%)	Indicative of HBV infection				Anti-HCV⁺ (%)	HBV⁺ and anti-HCV⁺ (%)
		HBsAg⁺ (%)	Anti-HBs⁺ (%)	Anti-HBc⁺ (%)	HBV⁺ (%)		
City							
Jilin	50	6 (12)	31 (62)	23 (46)	35 (70)	2 (4.0)	2 (4.0)
Shandong	50	5 (10)	24 (48)	21 (42)	33 (66)	0 (0)	0 (0)
Shaanxi	50	1 (2)	31 (62)	24 (48)	38 (76)	2 (4.0)	2 (4.0)
Total	150	12 (8)	86 (57)[c]	68 (45)	106 (71)	4 (2.7)	4 (2.7)
Village							
Jilin	50	3 (6)	19 (38)	22 (44)	27 (54)	1 (2.0)	1 (2.0)
Shandong	50	3 (6)	23 (46)	27 (54)	31 (62)	0 (0)	0 (0)
Shaanxi-A	50	5 (10)	21 (42)	31 (62)	35 (70)	0 (0)	0 (0)
Shaanxi-B	49	3 (6)	22 (45)	31 (63)	32 (65)	3 (6.1)	1 (2.0)
Total	199	13 (7)	85 (43)	111 (56)[b]	124 (62)	4 (2.0)	2 (1.0)
City+village							
Jilin	100	9 (9)	59 (50)	45 (45)	62 (62)	3 (3.0)	3 (3.0)
Shandong	100	8 (8)	47 (47)	48 (48)	64 (64)	0 (0)	0 (0)
Shaanxi	149	9 (6)	74 (50)	86 (58)	105 (70)	5 (3.4)	3 (2.0)
Total	349	25 (7)	121 (49)	179 (51)	230 (66)	8 (2.3)	6 (1.7)

No mark shows that difference in the prevalence is statistically insignificant ($p > 0.10$). Shandong and Shaanxi data are cited from Shimbo *et al* (1997) and Shimbo *et al* (1998), respectively. [b] is as under Table 1; [c] shows that the prevalence is higher ($p < 0.01$) in the marked group than in the counterpart group.

($0.05 < p < 0.10$) in the latter group than in the former. The overall evaluation of HBV⁺ prevalence did not differ between the two groups ($p > 0.10$) although the percentage tended to be greater for the city group (71%) than for the village group (63%).

Such was also the case for anti-HCV⁺; the rate for anti-HCV⁺ cases was greater for the city group (2.7%) than for the village group (2.0%) although the difference was statistically insignificant ($p > 0.10$). Further perusal of Table 2 suggests that the HBsAg⁺ prevalence varies substantially both in the cities (2 to 12%) and in the villages (6 to 10%), whereas the prevalence of anti-HBs⁺ and anti-HBc⁺ was rather even and high in all sites, so that the HBV⁺ prevalence was 66 to 76% in the cities and 54 to 70% in the villages. It is therefore possible to summarize that HBV infection rate in rural areas is probably no higher and might be even lower than that in urban areas, that the rates were high around 60 to 70% in both areas, and that the prevalence of HBsAg⁺ cases should also be comparable between the urban and the rural populations.

With regard to anti-HCV⁺ prevalence, the positivity rates were generally low, and no positive case was observed among the 50 examined cases in 3 sites out of 6 studied. It remains unclear if the observed (statistically insignificant) difference between the city group (4%) and the village group (2%) carries any epidemiological importance. Nevertheless, it appears prudent to deduce that the anti-HCV⁺ prevalence in the rural populations is no higher than the prevalence among the urban populations.

HBV and HCV infection rates published in the last decade are summarized in Table 3; in some studies (Liu *et al*, 1991; Qin *et al*, 1992; Tao *et al*, 1992; Deng *et al*, 1995; Shi *et al*, 1996; Li *et al*, 1998), subjects were of all ages, and the rates for 20⁺ year-old people were calculated by the present authors for better comparison by selecting ≥ 20 year-old people, because it is known that both HBV⁺ and HCV⁺ prevalence [and that of HCV⁺ in particular (Chen and Xia, 1999)] are lower in children than in adult populations.

With regard to HBsAg⁺ prevalence, Cao *et al* (1998) reported a high rate of 20% among the

Table 3
HBV marker-positive rates among adult general populations in China, as reported in literature.

Reference	Indicative of infection (%)[a]					Survey site[b]	Note
	HBV				HCV		
	A	B	C	D	E		
The present study	7	49	51	66	2.3	3 porvinces	Healthy urban and rural women
Seiji *et al* (1991a)	25	37	55	59	—	Shandong	Factory workers
Seiji *et al* (1991b)	4	37	38	44	—	Beijing	Factory workers
Seiji *et al* (1991c)	8	48	55	65	—	Shanghai etc	Factory workers
Liu *et al* (1991)[e]	11	38	49	69	—	4 provinces	20-60$^+$ y-old general population
Qin *et al* (1992)[e]	21	43	72	78	—	Shandong	20$^+$ y-old general population
Tao *et al* (1992)[e]	3	—	—	—	2.7	Beijing	20-60$^+$ y-old general population
Okuno *et al* (1994)	10	—	—	—	0	Guangxi	Healthy controls[c]
Ye *et al* (1994)	—	—	—	50	4.1	Jiansu	Healthy controls[c]
Deng *et al* (1995)[e]	23	20	72	81	1.9	Guangdong	20$^+$ y-old rural population
Qi and Wang (1995)	—	—	—	—	0.1	Beijing	Airport personnel
Wang *et al* (1995)	—	—	—	—	2.4	Shanxi	Urban population
Di (1996)	—	—	—	—	1.4	Jiansu	20$^+$ y-old general population
Hao *et al* (1996)	—	—	—	—	5.0	Sichuan	Blood donors
Shi and Bian (1996)[e]	—	—	—	—	2.5	Beijing	20$^+$ y-old urban population
Yao (1996)	10	—	—	43	—	China	A review
Zhao *et al* (1996)	7	—	—	34	—	Five provinces	General population
Zhou *et al* (1996)	—	—	—	—	1.4	Anhui	Healthy rural population
Liu *et al* (1997)	—	—	—	—	2.9	Shandong	1-59 y-old general population
Shimbo *et al* (1997)	8	47	48	64	—	Shandong	Healthy urban and rural women
Cao *et al* (1998)	20	31	54	—	1.7	Yangtze R[d]	Healthy controls[c]
Huang *et al* (1998)	—	—	—	—	1.9	Lioaoning	Patients with non-hepatic diseases
Li *et al* (1998)	15	37	75	84	4.3	Fujian	Healthy urban and rural populations
Shimbo *et al* (1998)	6	50	58	70	3.4	Shaanxi	Healthy urban and rural women
Zhang *et al* (1998)	5	—	—	—	3.5	Henan	Healthy controls[c]
Cui *et al* (1999)	8	—	—	—	11.5	Hebei	Rural population

— indicates that data are not available in the literature.
[a] A, HBsAg$^+$; B, anti-HBs$^+$; C, anti-HBc$^+$; D, HBV$^+$; E, anti-HCV$^+$.
[b] Name of province (or a large city) where the survey was conducted.
[c] Healthy controls to hepatocellular carcinoma patients.
[d] The inshore area of the Yangtze river.
[e] The rates were calculated by the present authors for 20$^+$ year-old populations.

people in the inshore area of the Yangtze river. The subjects were selected as controls matched to HCC patients, but no details of characteristics of the subjects were available for geographic identification. Qin *et al* (1992) also reported a high HBsAg$^+$ rate of 21% for a population (including farmers) in Shandong Province. Deng *et al* (1995) observed a high rate of 23% among an adult population in a rural area. A rate of 25% was reported by Seiji *et al* (1991a) among factory workers in a small city on the Yellow Sea coast. Otherwise, HBsAg$^+$ rates were generally in a range of 10% or less.

The anti-HBs$^+$ prevalence was in a range of 20% (Deng *et al*, 1995) to 49% (Table 2) and that of anti-HBc$^+$ was from 38% (Seiji *et al*, 1991b) to 75% (Li *et al*, 1998). The over-all prevalence of HBV$^+$ cases distributed from 34% (Zhao *et al*, 1996) in a five provinces study to 84% (Li *et al*, 1998) in Fujian Province, and the rate observed in the present study is also within this range. The

HBV^+ prevalence in the population studies by Cao *et al* (1998) with a high $HBsAg^+$ rate (20%) are most probably within this range, because anti-HBs^+ and anti-HBc^+ rates were not very high.

Considering the prevalence of anti-HCV^+ cases, the rates observed in the present study (*ie* 2.3% when the three provinces were combined and 0 to 3.4% when evaluated separately (Table 2) are well in the range of the values reported [*ie* 0% by Okuno *et al* (1994) among healthy controls to HCC cases in Guanxi Province to 4.3% by Li *et al* (1998) in Fujian Province], being in line with the estimate of 2 to 3% for overall Chinese populations (Tao *et al*, 1991; Mansell and Locarnini, 1995), and not contradictory to the understanding that HCV infection was less prevalent in the northwest (Li *et al*, 1993) and southern China (Okuno *et al*, 1994) as compared with the central part of the country.

With regard to the high prevalence issue, Hao *et al* (1996) reported a high HCV^+ rate of 5.0% for blood donors in Sichuan Province. This rate however should be evaluated with caution, because blood donation repeaters used to have a higher risk of hepatitis virus infection than the general population of the region (Di, 1996; Hao *et al*, 1996). No explanation is however available for exceptionally high HCV^+ prevalence (11.5%) in a rural population in Hebei Province (Cui *et al*, 1999).

The difference in HBV^+ and HCV^+ prevalence between the urban and rural populations was not substantial in the present study in northern China (Table 1), although there were some indications that the prevalence might be higher for urban populations rather than for rural populations (Table 2). In a large-scale study in Fujian Province in southern China, however, Li *et al* (1998) observed that the HBV^+ prevalence was significantly ($p < 0.01$) higher in rural populations than in urban populations, and that this was also the case for HCV^+ ($p < 0.05$). The urban-rural difference in HBV^+ and HCV^+ prevalence thus remains one of the foci of interest in this study group. Further analyses are currently in progress with special reference to comparison among northern, central and southern China.

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