PREVALENCE OF HEPATITIS B AND C INFECTION MARKERS AMONG ADULT WOMEN IN URBAN AND RURAL AREAS IN SHAANXI PROVINCE, CHINA

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Abstract. In an attempt to investigate possible urban-rural difference in prevalence of hepatitis B and C virus (HBV and HCV, respectively) infection in continental China, triplet surveys on HBV and HCV infection markers (*ie,* HBsAg, anti-HBs, anti-HBc, and anti-HCV) and serum enzyme levels (AST, ALT and γ-GTP) were conducted in 1997 on groups of apparently healthy adult women (49 to 50 subjects per group); one group (the City group) was in Xian, the provincial capital of Shaanxi Province, and two others (the Village A group and the Village B group) were in farming villages in the Province some 200 and 25 km away from Xian, respectively. Comparison among the three groups showed that there was no urban-rural difference in prevalence of HBV and HCV infection positive (HBV^+ and HCV^+) cases and that the overall prevalence of HBV^+ and HCV^+ cases was 70% and 3%, respectively. $HBsAg^+$ prevalence was however higher in the villages (8% when the two villages were combined) than in the city (2%). HBV infection was not associated in general with apparent increase in emission enzyme levels in the serum, whereas HCV infection might be associated with an increase in ALT, AST and γ-GTP. The present observation in combination with other previously published results suggests that urban-rural difference will not be remarkable in HBV and HCV infection prevalence in Continental China and that the public health problem is more serious with HBV infection and quite less so with HCV infection.

INTRODUCTION

Infection prevalence of two hepatitis viruses, hepatitis B virus (HBV) and hepatitis C virus (HCV), has been one of the foci in human virus epidemiology because both are well known risk factors of hepatocellular carcinoma (HCC) among people in Asia (Yuki *et al,* 1992; International Agency for Research on Cancer 1994; Okuno *et al,* 1994; Tsai *et al,* 1994a, b; Di Bisceglie, 1995; Mansell and Locarnini, 1995). Accordingly, this study group has been conducting seroepidemiology of these infections in continental China (Seiji *et al,* 1987, 1991a, b) where the incidence of HCC is known to be high (Qu 1986; Hu *et al,* 1986; Liu *et al,* 1991; Skolnick, 1996).

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A seroepidemiology study on HBV and HCV infection, although of a small scale, was conducted in Shaanxi Province in November 1997 with special reference to urban-rural comparison on the prevalence, because the living standard is assumed to be higher in urban areas than in rural areas when annual income and food habits are taken as parameters (Ge *et al,* 1996). The results are described in this article, and discussed in comparison with previous reports (Hu *et al,* 1986; Liu *et al,* 1991; Qin *et al,* 1992; Tao *et al,* 1992; Deng *et al,* 1995; Di, 1996; Zhao *et al,* 1996; Shi and Brian, 1996; Shimbo *et al,* 1998).

MATERIALS AND METHODS

Study population and study design

Surveys at three different regions were conducted in series in November, 1997; one is in Xian, the capital city of Shaanxi Province, China (better known by the historical name of Changan, the capital of Tang Dynasty of ancient Chinese Empire; to be called City), the second one in Bamiao Village (Village A) in Baoji County in the same province (some 200 km west to Xian), and the third one in Gongzhang Village (Village B) in Changan County also in the same province (some 25 km south-west to Xian). Xian is the center of administration, education and industrial activities, with living standard being better than that in the villages, *eg*, treated water supply being available there. The two villages are basically agricultural. Winter wheat and maize are staple products with additional production of green vegetables which are supplied to nearby towns as cash crop. The villagers depend on well water for daily life.

Non-smoking and non-habitually drinking adults were invited to participate in the study from women staff of a public health facility in Xian (50 women at the ages of 24 to 58 years), and from farming women in Village A (50 women at the ages of 21-55 years) and in Village B (49 women aged at 24 to 61 years). They were all married except for two in the City group. Blood samples were drawn from cubital vein 2 to 3 hours after breakfast.

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

Serum was separated on-site, kept chilled, and transferred to a clinical chemistry laboratory in Japan for analyses. HBV and HCV infection markers were assayed by commercial RIA or EIA kits, *ie*, HBV surface antigen (HBsAg) by AUSRIA® II-125, HBV core antibody (anti-HBc) by RIAKIT®, HBV surface antibody (anti-HBs) by AUSAB®, and HCV antibody (anti-HCV) by HCV EIA II (all from Abbott-Dinabot Co, Tokyo, Japan). The cut-off point for negativity was <1 for HBsAg and anti-HBs (as a cut-off ratio), less than 30% for anti-HBc (as a suppression rate) and <1 for anti-HCV (as a cut-off index); unless otherwise specified, borderline (*ie*,±) cases were taken as positive.

Other items studied 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. Among them, the findings of AST, ALT and γ-GTP were presented in this report as liver function markers. The normal range for the assays in the laboratory was 8 to 40 IU/l for AST, 5 to 35 IU/l for ALT and 0 to 60 IU/l for γ-GTP.

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 as parameters of distribution. Chi-square test and unpaired *t*-test (after logarithmic conversion when necessary) were employed for detection of difference in prevalence and in means, respectively.

RESULTS

HBV and HCV marker-positivity

Prevalence of cases positive to HBs antigen ($HBsAg^+$), HBs antibody ($anti\text{-}HBs^+$), HBc antibody ($anti\text{-}HBc^+$), any of the three HBV infection markers (HBV^+), or anti-HCV ($anti\text{-}HCV^+$) is given in Table 1, by the site of the study as well as the three sites in combination. As the median age of the whole study subjects was 40 years, the prevalence was also shown by two age sub-groups of ≤ 40 years and > 40 years.

Comparison between the two age sub-groups in the City group, the Village A group and the Village B group showed no age-dependent difference in the prevalence of $HBsAg^+$, $anti\text{-}HBs^+$, $anti\text{-}HBc^+$, HBV^+, $anti\text{-}HCV^+$ cases or the cases positive to both HBV and HCV ($p > 0.10$ by chi-square test). When the prevalence was compared among the three groups (*ie*, the two age sub-groups combined), the distribution of $HBsAg^+$ cases was not even among the three groups ($p < 0.01$), and the village group (8% for the Village A and B groups in combination) showed significantly ($p < 0.05$ by chi-square test) higher prevalence than the City group (2%). Comparison of HBV^+ prevalence showed, however, that there was no significant ($p > 0.10$) urban-rural difference in HBV infection prevalence, and $anti\text{-}HCV^+$ prevalence was also uniform ($p > 0.10$ for the difference).

When the subjects in the three regions were combined, no age-dependent difference was detected in any of the infection markers studied, with one exception that the difference in the prevalence

Table 1

Prevalence of hepatitis B and C virus infection markers in the three groups.

Study region	Age range (years)	No. of cases	Indicative of HBV infection: HBsAg⁺ (%)	Anti-HBs⁺ (%)	Anti-HBc⁺ (%)	HBV⁺ (%)	Anti-HCV⁺ (%)	HBV⁺ & anti-HCV⁺ (%)
City								
	21-40	25	0 (0)	17 (68)	10 (40)	18 (72)	0 (0)	0 (0)
	41-55	25	1 (4)	14 (56)	14 (56)	20 (80)	2 (8)	2 (8)
	Total	50	1 (2)	31 (62)	24 (48)	38 (76)	2 (4)	2 (4)
Village A								
	21-40	32	4 (13)	13 (41)	20 (63)	23 (72)	0 (0)	0 (0)
	41-55	18	1 (6)	8 (44)	11 (61)	12 (67)	0 (0)	0 (0)
	Total	50	5 (10)	21 (42)	31 (62)	35 (70)	0 (0)	0 (0)
Village B								
	21-40	28	1 (4)	14 (50)	19 (68)	19 (68)	1 (4)	1 (4)
	41-55	21	2 (10)	8 (38)	12 (57)	13 (62)	2 (10)	0 (0)
	Total	49	3 (6)	22 (45)	31 (63)	32 (65)	3 (6)	1 (2)
City + Villages								
	21-40	85	5 (6)	44 (52)	49 (58)	60 (71)	1 (1)	1 (1)
	41-55	64	4 (6)	30 (35)	37 (44)	44 (52)	4 (6)[a]	2 (3)
	Total	149	9 (6)[b]	74 (50)[c]	86 (58)	104 (70)	5 (3)	3 (2)

Abbreviations: HBsAg, HBV antigen; anti-HBs, HBV surface anti-body: anti-HBc, HBV core antibody: anti-HCV, HCV antibody. The values are the number of cases (% in parentheses). Unless otherwise specified, 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 three regional groups (the two age groups combined, or total).

[a] Difference in the prevalence between the two age groups was of borderline significance (0.10>p>0.05 by chi-square test).

[b] Difference among the three regions was statistically significant (p<0.01 by chi-square test). The difference between the City group and the Village group (*ie,* the Village A and B groups in combination; n=99) was also significant (p<0.05).

[c] Difference among the three groups was of borderline significance (0.10>p>0.05 by chi-square test).

of anti-HCV⁺ cases was of borderline significance ($0.10 > p > 0.05$). Thus, the overall prevalence of HBsAg⁺, HBV⁺, and HCV⁺ cases was 6%, 70% and 3%, respectively. It should be noted that three women were positive to both HBV and HCV infection. One of them was a 28 year-old woman in the Village B group, and remaining two were both 43 year-old women in the City group. One of the 43 year-old women had elevated AST (86 IU/l) and ALT (147 IU/l), whereas both AST and ALT remained normal (*ie,* <20 IU/l) in other two cases (*ie,* a 28 year-old woman and a 43 year-old woman).

Liver function and HBV or HCV positivity

A total of 149 cases were classified into two groups of those positive (including borderline-positive) to HBsAg, HBV or HCV, and those negative to each marker, and GM (GSD) values for of AST, ALT and γ-GTP, respectively, were calculated for each group (Table 2). Comparison after logarithmic conversion showed that there was no significant difference in the levels of AST, ALT and γ-GTP between the HBsAg⁺ and HBsAg⁻ groups or the HBV⁺ and HBV⁻ groups. In case of HCV

Table 2

Serum enzyme activity by positivity to HBV infection markers.

Serum enzyme	Pos/neg	HBV or HCV infection marker HBsAg	HBV	HCV
Number of cases	Positive	9	105	5
	Negative	140	44	144
AST	Positive	26.5 (1.53)	25.3 (1.42)	30.8 (2.00)[b]
	Negative	25.0 (1.38)	24.7 (1.31)	24.9 (1.37)
ALT	Positive	28.3 (1.81)	23.8 (1.80)	36.4 (2.97)[a]
	Negative	23.7 (1.78)	24.5 (1.76)	23.6 (1.74)
γ-GTP	Positive	10.1 (1.34)	11.8 (1.68)	15.8 (1.78)[b]
	Negative	11.7 (1.69)	11.0 (1.66)	11.4 (1.67)

Values are GM (GSD) of enzyme activity for the three regional groups in combination.
Superscript letters show statistical significance of the differences between the positive and negative cases ([a] and [b] for p <0.01 and 0.10>p>0.05, respectively, by unpaired Student's *t*-test after logarithmic conversion).

Table 3

Cases of elevated serum activity by positivity to HBV and HCV infection markers.

Elevated serum enzyme activity	HBV infection Pos	Neg	Total	HCV infection Pos	Neg	Total
No. of cases	105	84	149	5	144	149
AST	11	2	13	2[b]	11	13
ALT	27	11	38	2	36	38
γ-GTP	2	1	3	0	3	3
AST and ALT[a]	11	2	13	2[b]	11	13

Unless otherwise specified, there was no significant difference (p>0.10) in the prevalence of cases with elevated enzyme activities between HBV^+ and HBV^- (or, between HCV^+ and HCV^-) cases.
[a] Both AST and ALT were elevated.
[b] Difference in the prevalence between HCV^+ and HCV^- cases was statistically significant (p<0.01 by chi-square test).

infection, the HCV^+ group had significantly ($p < 0.01$) higher ALT levels than the HCV^- group, and the differences in AST and γ-GTP levels were of borderline significance ($0.10 > p > 0.05$), suggesting that the ALT activity, and possibly that of AST and γ-GTP, were elevated due to HCV infection.

In a further analysis, the 149 cases were classified by the positivity (including borderline positive cases) to HBV or HCV infection, and the cases with higher than normal (*ie,* above the upper normal range) AST, ALT or γ-GTP activity, respectively, were identified (Table 3). Comparison by chi-squre test showed the the prevalence of elevated activity cases was independent of HBV infection (the left half in Table 3), whereas the cases with elevated AST level was more prevalent in HCV^+

Table 4

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

Year[a]	Positivity (%) [b]			Survey site[c]	Population	Ref[d]
	HBsAg⁺	HBV⁺	HCV⁺			
1986	10	43	–	Whole China	General populaton	A
1991	10-13	58-73	–	Four provinces	20-60⁺ y-old people	B
1992	21	79	–	Shandong	≥ 20 y-old people	C
1992	3	–	2.7	Beijing	20-60⁺ y-old peole	D
1995	–	–	1.9	Guangdong	≥ 20 y-old people	E
1996	–	–	1.4	Jiangsu	≥ 20 y-old people	F
1996	7	34	–	Five provinces	General population	G
1996	–	–	2.5	Beijing	≥ 20 y-old people	H
1997	8	64	0.0	Shandong	Healthy women	I
1998	6	70	3.3	Shaanxi	Healthy women	J

Only those on adult population and assayed by RIA or RPHA are cited. Unless otherwise specified, the prevalence is for the two sexes combined.

[a] Year of publication.

[b] Abbreviations are: $HBsAg^+$, positive to HBs antigen; HBV^+, positive to any of the three HBV infection markers; HCV^+, positive to HCV antibody.

[c] Name of Province (or a large city) surveyed.

[d] References are: A, Hu *et al* (1986); B, Liu *et al* (1991); C, Qin *et al* (1992); D, Tao *et al* (1992); E, Deng *et al* (1995); F, Di (1996); G. Zhao *et al* (1996); H, Shi *et al* (1996); I, Shimbo *et al* (1997); J, The present study.

cases than in HCV^- cases. It should also be noted that the cases with elevated levels both in AST and ALT were more ($p < 0.01$) prevalent in HCV^+ women (2 out of 5, or 40%) than HCV^- women (11 out of 144, or 8%).

DISCUSSION

The present triplet surveys (one in urban and two in rural regions) in the same province of Shaanxi showed that there was no urban-rural difference in HBV and HCV infection prevalence and that the overall prevalence of HBV^+ and HCV^+ cases was 70% and 3%, respectively (Table 1). The prevalence of $HBsAg^+$ cases was however higher in the villages (8%) than in the city (2%). Overall, the HBV infection was not accompanied by apparent liver function abnormalities, whereas HCV infection was associated with an increase in ALT, and possibly also in AST and in γ-GTP (Tables 2 and 3).

The present findings are in general agreements with the previous observation by this study group in a paired regions of a provincial capital and a farming village in the vicinity in Shandong Province (Shimbo *et al,* 1997) in the sense that HBV infection rate may request serious attention in public health (because the $HBsAg^+$ prevalence was 6% in the present study and 8% in the previous study, and that of HBV^+ cases was 70% and 64%, respectively) whereas HCV infection is less serious with prevalence being low (*ie,* 3% and 0%, respectively). HBV and HCV prevalence rates among adult people in continental China have been reported in various publications (Hu *et al,* 1986; Liu *et al,* 1991; Qin *et al,* 1992; Tao *et al,* 1992; Deng *et al,* 1995; Di, 1996; Zhao *et al,* 1996; Shi *et al,* 1996; Shimbo *et al,* 1997) as summarized in Table 4. It is evident that only few authors (Tao *et al,* 1992; Shimbo *et al,* 1997) examined both HBV and HCV infection on the same subjects and in parallel. Nevertheless, it is possible to observe that HBV^+ rates were 34 to 73% depending on the areas studied whereas HBsAg-positivity was 10% or less [with one exception of Qin *et al* (1992) who reported a prevalence of as high as 21% among residents in Shandong Province], and that HCV^+ prevalence was 3% or even less independent of the provinces studied. The observation as a whole suggests that the major public health issue is on HBV infection rather than HCV infection in continental China, when threats by the two hepatitis viruses are compared.

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