URBAN-RURAL COMPARISON OF HBV AND HCV INFECTION PREVALENCE AMONG ADULT WOMEN IN SHANDONG PROVINCE, CHINA

Shinichiro Shimbo[1], Zuo-Wen Zhang[2], Jiang-Bin Qu[3], Ji-Jun Wang[3], Chun-Ling Zhang[3], Li-Hua Song[4], Takao Watanabe[5], Kae Higashikawa[6] and Masayuki Ikeda[6]

[1]Department of Food and Nutrition, Kyoto Women's University, Kyoto 605, Japan; [2]Department of Public Health, Faculty of Medicine, Kyoto University, Kyoto 606-01, Japan; [3]Department of Hygiene, Faculty of Public Health, Shandong Medical University, Jinan 250012, Shandong, China; [4]Health Bureau, Zhangqiu City, Zhangqiu 250200, Shandong, China; [5]Miyagi University of Education, Sendai 980, Japan; [6]Kyoto Industrial Health Association, Kyoto 604, Japan

Abstract. In order to make urban-rural comparison of the prevalence of hepatitis B and C virus (HBV and HCV, respectively) infection in China, a twin survey was conducted in 1996 on two groups (50 subjects each) of 21-55 year-old, apparently healthy women for infection markers and serum enzyme levels; one group (the urban group) was in Jinan, the provincial capital of Shandong Province, and the other (the rural group) was in a farming village in Zhangqiu area some 30 km away from Jinan City. Comparison between the two groups showed that there was no significant ($p>0.10$) difference in the prevalence of $HBsAg^+$, anti-HBs^+, anti-HBc^+ and the cases positive to any of the three HBV infection markers (*ie* HBV^+). No age-dependent difference was detected within or between the groups. Thus the overall positivity rate was 8% for $HBsAg^+$, 47% for anti-HBs^+, 48% for anti-HBc^+, and 64% for HBV^+. No anti-HCV^+ case was found either in the urban group or in the rural group. Liver function remained normal in all cases studied. The results together with perusal of published data suggest the urban-rural difference will not be remarkable, if present, in HBV and HCV infection in the regions studied, and possibly in China as a whole.

INTRODUCTION

Infection of hepatitis B virus (HBV) and that of hepatitis C virus (HCV) are well known risk factors of hepatocellular carcionoma (HCC) among people in some areas in Asia such as Japan, continental China and Taiwan (Yuki *et al,* 1992; Okuno *et al,* 1994; Tsai *et al,* 1994a, b; Di Bisceglie, 1995; Mansell and Locarnini, 1995). Continental China is among the areas of high HCC incidence, and extensive seroepidemiological studies, especially on HBV infection (Qu, 1986; Hu *et al,* 1986; Liu *et al,* 1991; Skolnick, 1996), have been carried out throughout the vast country or over several provinces, and it was concluded that the HBV infection rates are generally high, although varied, depending on the regions in the country. Whereas a majority of the population in continental China live in rural areas, it is not yet clear, however, if the endemic rate is similar in towns and villages, or if the rate is higher among villagers than among urban inhabitants.

An exploratory survey, although small in scale, was launched by this study group to obtain answers to this important question. The survey was designed to examine two comparable groups of inhabitants on HBVand HCV infection prevalence rates, one group in a provincial capital and the other in a farming village.

Correspordence : Masayuki Ikeda, Kyoto Industrial Health Association, 67 Nishinokyo-Kitatsuboicho, Nakagyo-ku, Kyoto 604, Japan. Tel: +81-75-823-0533; Fax: +81-75-802-0038

MATERIALS AND METHODS

Study population and study design

A twin survey was conducted in October, 1996, one in the provincial capital of Jinan City in Shandong Province, China and the other in a farming village of Baiquan in Zhangqiu area some 30 km east to the city. A group of 50 women teaching staff in Shandong Medical University in Jinan (the urban group) and 50 farming women in the village (the rural group) volunteered to join the study; women in the rural group were matched by age to the urban group women with an allowance of 3 year difference in age. They were in the age range of 21-55 years, and mostly married; no occupational blood donors were included. They offered blood samples and had a clinical interview (at the time of blood sampling) for information on daily life such as water supply and personal habits of smoking and drinking. Blood samples were drawn from cubital vein 2.5-3 hours after taking any foods or drinks.

Women rather than men were chosen because sex difference in HCC prevalence in China is known (Yuan *et al,* 1995), although HBV (Qin *et al,* 1992) and HCV (Shi and Bian, 1996) infection rates may not differ substantially between the two sexes. Taking the small size of the survey into consideration, only nonsmoking and non-habitually drinking women were selected for better comparability of the two groups.

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

Assays for infection markers of hepatitis B and C virus (HVB and HVC, respectively) were 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). Serum enzyme activities were assayed by conventional methods.

Statistical analysis

A normal distribution was assumed for infection markers, and therefore arithmetic means (AMs) and standard deviations (ASDs) were calculated as statistical parameters. In case of serum enzyme activities, a log-normal distribution was assumed so that geometric means (GMs) together with geometric standard deviations (GSDs) were calculated. Chi-square test and unpaired Student's *t*-test were employed for detection of difference in prevalence and in means, respectively.

RESULTS

HBV and HCV marker-positivity

The number of cases positive for HBV surface antigen ($HBsAg^+$), HBV surface antibody (anti-HBs^+), HBV core antibody (anti-HBc^+), any of the three HBV infection markers (HBV^+), or HCV antibody (anti-HCV^+) are summarized in Table 1. The prevalence is presented by survey site and also as the two sites combined, as well as by age group of nearly equal size (*ie* taking 40 years of age as a point of division) and as all ages.

Comparison of the prevalence was conducted between the 21-40 year-old and 41-55 year-old groups for $HBsAg^+$, anti-HBs^+, anti-HBc^+ and HBV^+. No significant ($p > 0.10$) difference was detected between the two age groups either in the urban group or in the rural group (Table 1). A similar comparison of the same age groups in the city and in the village also failed to detect any significant ($p > 0.10$) difference in prevalence of $HBsAg^+$, anti-HBs^+, anti-HBc^+ or HBV^+ cases, except that the prevalence of anti-HBc^+ cases in the 21-40 year-old group in the city (30%; 6 cases out of 20) examined was barely ($0.05 < p < 0.10$) lower than that in the village (55%; 16 cases out of 29).

When the urban group was compared with the rural group (two age-dependent subgroups combined in either group), there was no significant ($p > 0.10$) difference in the prevalence of $HBsAg^+$, anti-HBs^+, anti-HBc^+ or HBV^+. Thus, the overall positivity rate when all cases in the two survey sites were combined was 8% for $HBsAg^+$, 47% for anti-HBs^+, 48% for anti-HBc^+, and 64% for HBV^+, indicating that only one-third of the women surveyed were free from HBV infection. In a sharp contrast, none of the women surveyed were positive to HCV infection, independent of the place of residence or of the age.

Liver function

Liver function tests included AST, ALT and γ-GTP. Table 2 summarizes comparison of the three enzyme activity levels between marker-positive and -negative groups. No significant difference was found in most cases, except that AST and ALT activities were significantly ($p < 0.05$) higher in the HBV^+ group than in the HBV^- group. Moreover, no case exceeded the upper limit of 40 IU/l for AST, 35 IU/l for ALT, and 60 IU/l for γ-GTP when the activities were compared with the normal ranges of the test laboratory, indicating that liver function remained normal, regardless of positive or negative

Table 1

Prevalence of hepatitis B and C virus infection markers in the two populations.

Study region / Age range (years)	No. of cases	Indicative of HBV infection				HBV⁻	Anti-HCV⁺
		HBsAg⁺	Anti-HBs⁺	Anti-HBc⁺	HBV⁺		
City							
21-40	20	3 (15%)	10 (50%)	6[a] (30%)	13 (65%)	7 (35%)	0 (0%)
41-55	30	2 (7%)	14 (47%)	15 (50%)	20 (67%)	10 (33%)	0 (0%)
Total	50	5 (10%)	24 (48%)	21 (42%)	33 (66%)	17 (34%)	0 (0%)
Village							
21-40	29	2 (7%)	12 (41%)	16[a](55%)	18 (62%)	11 (38%)	0 (0%)
41-55	21	1 (5%)	11 (52%)	11 (52%)	13 (62%)	8 (38%)	0 (0%)
Total	50	3 (6%)	23 (46%)	27 (54%)	31 (62%)	19 (38%)	0 (0%)
City + Village							
21-40	49	5 (10%)	22 (45%)	22 (45%)	31 (63%)	18 (37%)	0 (0%)
41-55	51	3 (9%)	25 (49%)	26 (51%)	33 (65%)	18 (35%)	0 (0%)
Total	100	8 (8%)	47 (47%)	48 (48%)	64 (64%)	36 (36%)	0 (0%)

Abbreviations: 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). Unless otherwise specified, there is no significant ($p>0.10$) difference in the prevalence of HBsAg⁺, anti-HBs⁺, anti-HBc⁺ or anti-HCV⁺ between the urban group and the rural group (the 21-40 year-old women, the 41-55 year-old women and the combination), or between the 21-40 year-old and the 41-55 year-old women (in the city, the village or the combination) as assayed by chi-squares test.

[a] The difference in the prevalence in anti -HBc⁺ between the 21-40 year-old women in the urban group (6 cases out of 20 women) and their counterparts in rural group (16 out of 29) is barely significant ($0.05 < p < 0.10$).

Table 2

Serum enzyme activity by positivity to HBV infection markers.

Serum	RBV infection marker				
	Pos/neg	HBsAg	Anti-HBs	Anti-HBc	HBV
Number of cases	Positive	8	47	48	64
	Negative	92	53	52	36
AST	Positive	17.5 (1.38)	18.6 (1.27)	18.8 (1.24)	18.4 (1.28)*
	Negative	17.8 (1.25)	17.2 (1.26)	16.9 (1.27)	16.9 (1.23)
ALT	Positive	17.8 (1.67)	14.7 (1.44)	14.7 (1.39)	14.9 (1.46)*
	Negative	14.0 (1.47)	13.7 (1.52)	13.5 (1.63)	13.0 (1.53)
γ-GTP	Positive	8.3 (1.17)	8.5 (1.50)	8.6 (1.42)	8.3 (1.42)
	Negative	10.5 (2.83)	8.6 (1.39)	8.5 (1.46)	8.9 (1.46)

Unless otherwise specified, values are GM (GSD) of enzyme activity for the urban and rural groups in combination. Asterisks show statistical significance of the differences between the positive and negative cases (* for $p<0.05$).

HBV infection.

DISCUSSION

The present survey on adult women made it clear that the prevalence of HBsAg⁺, anti-HBs⁺, anti-HBc⁺ and HBV⁺ cases did not differ (Table 1) between inhabitants of a provincial capital and farmers in an agricultural village, although the way of life in the two survey sites was substantially different, *eg,* the people in the city have a supply of treated water, whereas the villagers depend on their own well water (information obtained in a clinical interview). Substantial differences in food consumption pattern were also found (to be described in a separate paper: Qu *et al,* 1997). In brief, women in the village took sigificantly less lipid and more carbohydrate than their counterparts in the city, although there was no significant difference in total energy and protein intake.

It is quite conceivable that no age effects on HBV marker prevalence were observed among adult women in the city or in the village because both vertical and horizontal HBV transmission will take place early in life (Yao, 1996), except for iatrogenic infection. Another and even more striking observation is the absence of anti-HCV⁺ cases both in the urban group and in the rural group (Table 1). This conclusion should be taken as preliminary, however, because the scale of the survey is not large enough to allow detailed statistical as well as life style-linked analysis.

HBV infection prevalence in continental China as reported in the literature is summarized in Table 3, in which only the results assayed by the RIA or RPHA method are quoted for better comparability in detection sensitivity. Seiji *et al* (1991a), Tao *et al* (1992) and Zhao *et al* (1996) reported low HBsAg⁺ prevalence (or low HBV⁺ prevalence in combination) among factory workers in Beijing, general populations in Beijing or in five provinces, respectively, whereas Qin *et al* (1992) observed very high HBsAg⁺ and HBV⁺ rates (20% and 79%, respectively) in a small city at the eastern end of the Shandong peninsula (thus in the same province of the present study, but more than 500 km distant). Otherwise, the prevalence observed in the present study (*ie* 8% for HBsAg⁺ and 64% for HBV⁺, both in urban and rural women; Table 1) can be taken as

Table 3

HBV marker-positive rates among general populations in China, as reported in literature[a].

Reference	Indicative of HBV infection (%)				Notes	
	HBsAg⁺	Anti-HBs⁺	Anti-HBc⁺	HBV⁺	Survey site[b]	Note
The present study	8	47	48	64	Shandong	Healthy urban and rural women
Hu *et al* (1986)	10	-	-	43	Whole China	General population
Seiji *et al* (1987)	8	46	-	53	Anhui	Factory workers
Seiji *et al* (1991a)	4	37	38	44	Beijing	Factory workers
Seiji *et al* (1991b)	8	48	55	65	Shanghai etc	Factory workers
Liu *et al* (1991)	10	32	45	58	Four prov	0-60⁺ y-old general pop
Ibid	10-13	34-39	45-56	58-73	Four prov	20-60⁺ y-old general pop
Qin *et al* (1992	20	45	73	79	Shandong	0-50⁺ y-old general pop
Ibid	21	44	73	79	Shandong	≥ 20 y-old general pop
Tao *et al* (1992)	3	-	-	-	Beijing	0-60⁺ y-old general pop
Ibid	3	-	-	-	Beijing	20-60⁺ y-old general pop
Okuno *et al* (1994)	10	-	-	-	Guangxi	Healthy controls[c]
Ye *et al* (1994)	-	-	-	50	Jiansu	Healthy controls[c]
Zhao *et al* (1996)	7	-	-	34	Five prov	General populations

Abbreviations: HBsAg, HBV antigen; anti-HBs, HB surface antibody; anti-HBc, HB core antibody; anti-HCV, HCV antibody.

[a] Only those assayed by RIA or RPHA methods are cited.

[b] Name of province (or a large city) surveyed.

[c] Healthy controls to hepatocellular carcinoma patients.

Table 4

Anti-HCV antibody-positive rates among general populations in China, as reported in literature[a].

Reference	Anti-HCV$^+$ rate(%)	Survey site[a]	Note
The present study	0	Shandong	Healthy urban and rural women
Tao *et al* (1991)	2.1	Beijing	General urban population
Tao *et al* (1992)	2.1	Beijing	0-60$^+$ y-old general population
Ibid	2.7	Beijing	20-60$^+$ y-old general population
Okuno *et al* (1994)	0	Guangxi	Healthy controls[b]
Ye *et al* (1994)	4.1	Jiansu	Healthy controls[b]
Deng *et al* (1995)	1.0	Guangdong	1-59 y-old rural population
Ibid	1.9	Guangdong	≥ 20 y-old general population
Qi *et al* (1995)	0.9	Beijing	Airport attendants
Wang *et al* (1995)	4.6	Shanxi	Students, etc
Di *et al* (1996)	2.0	Jiangsu	0-60$^+$ y-old general population
Ibid	1.4	Jiangsu	≥ 20 y-old general population
Hao *et al* (1996)	0.8	Xian	Pregnant women
Shi *et al* (1996)	2.6	Beijing	0-60$^+$ y-old general popultion
Ibid	2.5	Beijing	≥ 20 y-old general population
Zhou *et al* (1996)	1.4	Anhui	Farmers
Ibid	0.5	Anhui	Coal miners

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

typical for the general population when compared with reported results (Seiji *et al*, 1987, 1991b; Hu *et al*, 1986; Okuno *et al*, 1994; Ye *et al*, 1994; Yao, 1996). It should be added that no substantial difference in the prevalence was observed when younger (≤19 year-old) people were excluded from the populations surveyed, *eg* in case of Yao (1996).

It was not possible from the literature survey to identify whether the reported values are for urban or rural populations. It may be feasible, however, to estimate that factory workers (Seiji *et al*, 1987, 1991b) and healthy controls in studies of HCC (Okuno *et al*, 1994; Ye *et al*, 1994) were from cities, whereas the populations surveyed by Liu *et al* (1994) and Zhao *et al* (1996) appear to include both urban and rural populations. With such assumptions, it appears likely that the urban-rural difference in the prevalence of HBV infection is not substantial, because HBV$^+$ prevalence was 40-53% in assumedly urban populations (Seiji *et al*, 1987, 1991b; Ye *et al*, 1994) whereas it was 34-58% for the probable mixture of urban and rural populations (Liu *et al*, 1991; Zao *et al*, 1996). In this connection, Qu (1986) observed that both HBsAg$^+$ and anti-HBs$^+$ prevalences were higher in rural areas (10.3%, and 4.1%, respectively) than in urban areas (8.1% and 3.1%) in a nation-wide large-scale survey. Variation was wide among the provinces (*ie* from 3.8% in Shanxi Province to 14.9% in Fujian Province in HBsAg$^+$ prevalence, and from 1.2% in Xizhang Autonomous Region to 7.7% in Hunan Province in anti-HBs$^+$ prevalence), and no rural-urban matching was made in the evaluation of the results.

A growing number of papers on anti-HCV$^+$ prevalence in continental China have been published in recent years. Review of the papers (Tao *et al*, 1991; Okuno *et al*, 1994; Ye *et al*, 1994; Deng *et al*, 1995; Qi *et al*, 1995; Wang *et al*, 1995; Di *et al*, 1996; Hao *et al*, 1996; Shi *et al*, 1996; Zhou *et al*, 1996) shows that the reported prevalence of anti-HCV$^+$ cases is distributed in a range of zero (Okuno *et al*, 1994) to 4.6% (Wang *et al*, 1995). The rates, less than 5% at highest (Wang *et al*, 1995), are in an agreement with each other in the sense that HCV infection is much less common than that of HBV in continental China. The observation is further in line with the findings that the anti-HCV$^+$ prevalence is low among chronic liver disease patients in northwest China (Li *et al*, 1993) and also among

HCC patients in southern China (Okuno *et al,* 1994). In addition, the observation not only supports the conclusion by Okuno *et al* (1994) that HBV infection rather than HCV infection plays an important etiological role in the development of HCC in southern China, but suggests that the conclusion may be extrapolated to other parts of continental China.

Regarding low anti-HCV$^+$ prevalence, it is of interest to point out that in Taiwan where anti-HCV$^+$ prevalence is low (Liu *et al,* 1991), no interaction was observed between HBV infection and HCV infection (Chang *et al,* 1992; Tsai *et al,* 1994a, c). Moreover, the contribution of HBV infection to the risk for HCC is several times greater than that of HCV infection for the people in Taiwan (Tsai *et al,* 1994b), although HCV infection rate could be exceptionally high under specific social conditions such as aboriginal communities (Wu *et al,* 1992).

Considering possible urban-rural difference in anti-HCV$^+$ prevalence, perusal of the papers cited in Table 4 shows that some authors [*eg* Deng *et al* (1995) and Zhou *et al* (1996)] surveyed people in villages whereas others [*eg* Qi *et al* (1995) and Shi *et al* (1996)] studied people in a large city like Beijing. The subjects studied by Okuno *et al* (1994) and Ye *et al* (1994) as healthy controls for HCC patients were most probably also from cities. The anti-HCV$^+$ prevalence reported by Deng *et al* (1995), *ie* 1.0 to 1.9% depending on age groups and Zhou *et al* (1996) of 1.4% for farmers are comparable to the prevalence reported for urban populations, *ie,* from 0.8% by Ha *et al* (1996) to 2.6% by Shi *et al* (1996), which as a whole agree with the present observation (Table 4) that HCV infection prevalence is low and that there will be no substantial urban-rural difference in anti-HCV$^+$ prevalence.

ACKNOWLEDGEMENTS

This work was supported in part by a research grant for 1996 (Grant No, 08044167: Principal investigator; T Watanabe) from the Ministry of Education, Science, Sports and Culture, the Government of Japan to SS and TW.

REFERENCES

Chang WY, Chen CJ, Lu SN, *et al.* Relationship between fatty liver, alanine aminotransferase, HBsAg and hepatitis C virus. *J Gastroenterol Hepatol* 1992; 7: 455-8

Deng GH, Xie WY, Wu BS, Zheng QG. Seroepidemiological study on viral hepatitis in Nanxong County. *Guangdong Sanit Epidemiol Prev* 1995; 21 (1) : 26-8 (in Chinese).

Di Bisceglie AM. Hepatitis C and hepatocellular carcinoma. *Sem Liv Dis* 1995; 15: 64-9.

Di L. A seroepidemiological investigation on hepatitis C. *Modern Prev Med* 1996; 23 (1): 55-6 (in Chinese with English abstract).

Hao F, Li MD, Thaler MM, Chen GZ. Prevalence and significance of single serum antibody response to hepatitis C virus core antigen among various populations. *Chin J Infect Dis* 1996; 14 (3) : 141-3 (in Chinese).

Hu ZH, Qu ZY, Jing Q, Ding ZR, *et al.* The overall infection rate of HBV in Chinese general population by sampling investigation. *Chin J Microbiol Immunol* 1986; 6: S70-S77.

Li X, Hayashi N, Yuki N, *et al.* Low prevalence of hepatitis C virus antibodies in chronic liver disease in northwest China. *J Med Virol* 1993; 41: 247-50.

Liu CB, Xu ZY, Cao HL, *et al.* Sero-epidemiology of HBV infection in four provinces in China. *Chin J Virol* 1991; 7: S8-S14.

Mansell CJ, Locarnini SA. Epidemiology of hepatitis C in the East. *Sem Liv Dis* 1995; 15: 15-32.

Okuno H, Xie ZC, Lu BY, *et al.* A low prevalence of anti-hepatitis virus antibody in patients with hepatocellular carcinoma in Guangxi Province, southern China. *Cancer* 1994; 73: 58-62.

Qi GZ, Wang Z. HCV infection prevalence among the people in Beijing Capital Airport area. *Chin J Epidemiol* 1996; 16 (6) : 327 (in Chinese).

Qin XZ, Wang ES, Wang SP, Chao SW. Prevalence of HAV and HBV infection markers among general population in Rongcheng City. *Shandong Sanit Epidem Prev* 1992; 12 (4) :230-2 (in Chinese).

Qu ZY. An epidemiological study on the distribution of HBsAg and anti-HBs in China. *Chin J Microbiol Immunol* 1986; 6: S20-S40.

Qu JB, Zhang ZW, Xu GF, *et al.* Urban-rural comparison of nutrient intake by adult women in China. *Tokoku-J Exp Med,* 1997 (in press).

Seiji K, Inoue O, Kasahara M, *et al.* Prevalence of serological hepatitis B markers in a working population in Hefei, China. *Asia-Pacif J Public Health* 1987; 1: 28-33.

Seiji K, Liu SJ, Xu XP, *et al.* Prevalence of hepatitis B infection markers among factory workers in Beijing, China. *Asia-Pacif J Pubic Health* 1991a; 5: 345-9.

Seiji K, Inoue O, Watanabe M, *et al.* Hepatitis B virus prevalence in industrialized cities in China. *Asia-Pacif J Public Health* 1991b; 5: 350-8.

Shi YR, Bian XL. HCV infection prevalence in general populations in Beijing. *Chin J Public Health* 1996; 12 (5) : 199-201 (in Chinese).

Skolnick AA. Armed with epidemiologic research, China launches programs to prevent liver cancer. *J Am Med Assoc* 1996: 276; 1458-9.

Tao QM, Wang Y, Wang H, *et al.* Seroepidemiology of HCV and HBV infection in northern China. *Gastroenterol Jpn* 1991; 26 (Suppl 3): 156-8.

Tao QM, Wang Y, Wang H, Chen WR, Sun Y, Meng Q. Preliminary report on seroepidemiology of HCV and HBV infection in northern China. *Chin Med J* 1992; 105: 209-11.

Tsai JF, Chang WY, Jeng JE, Ho MS, Lin ZY, Tsai JH. Effects of hepatitis C and B viruses infection on the development of hepetocellular carcinoma. *J Med Virol* 1994a; 44: 92-5.

Tsai JF, Jeng JE, Ho MS, Chang WY, Lin ZY, Tsai JH. Hepatitis B and C virus infection as risk factors for hepatocellular carcinoma in Chinese: A case-control study. *Int J Cancer* 1994b; 56: 619-21.

Tsai JF, Chang WY, Jeng JE, Ho MS, Tsai JH. Hepatitis B and C virus infection as risk factors for liver cirrhosis and cirrhotic hepatocellular carcinoma; a case-control study. *Liver* 1994c; 14: 98-102.

Wang JS, Zhang ZM, Guo RQ, Xue WY, Xu SL. HCV antibody survey in healthy general population and blood products in Taiyuan City. *Chin J Public Health* 1995; 11: 73-4 (in Chinese).

Wu JS, Lu CF, Chou WH, Chen HY, Lee HF, Wu YC, Lin SY. High prevalence of hepatitis C virus infection in aborigines in Taiwan. *Jpn J Med Sci Biol* 1992; 45: 165-74.

Yao GB. Importance of perinatal versus horizontal transmission of hepatitis B virus infection in China. *Gut* 1996: 38 (Suppl 2): S39-S42.

Ye BF, Shen J, Xu YC, Niu JT, *et al.* Etiological study on the relationship between HBV, HCV and HCC. *Chin J Epidemiol* 1994; 15 (3) : 131-4 (in Chinese, English abstract).

Yuan JM, Ross RK, Stanczyk FZ, *et al.* A cohort study of serum testosterone and hepatocellular carcinoma in Shanghai, China. *Int J Cancer* 1995; 63: 491-3.

Yuki N, Hayashi N, Kasahara A, *et al.* Hepatitis B virus markers and antibodies to hepatitis C virus in Japanese patients with hepatocellular carcinoma. *Digest Dis Sci* 1992; 37: 65-72.

Zhao QM, Zhou YS, Linan ZH, Li JY, Zhan XT, Jiang CL. Epidemiological study on HDV infection in some areas in China. *Chin J Public Health* 1996; 12 (5): 197-8 (in Chinese).

Zhou YS, Zhao QM, Wang FY, *et al.* HCV infection prevalence and HCV genotypes. *Chin J Public Health* 1996; 12 (5) : 204-5 (in Chinese).