

Prevalence of hepatitis C virus and hepatitis B virus infections in HIV-positive Chinese patients

Y. X. YAN^{1†}, Y. Q. GAO^{2†}, X. SUN², W. WANG¹, X. J. HUANG², T. ZHANG², M. LI¹,
C. P. ZANG³, Z. C. LI^{2*} AND H. WU^{2*}

¹ Department of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Capital Medical University, Beijing, China

² STD and AIDS Clinical Center, Beijing Youan Hospital, Capital Medical University, Beijing, China

³ National Center for AIDS/STD Prevention and Control, Chinese Center for Disease Control and Prevention, Beijing, China

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SUMMARY

To evaluate the prevalence of hepatitis C virus (HCV) and/or hepatitis B virus (HBV) infections in HIV-infected patients in China, an epidemiological serosurvey was conducted from May 2007 to September 2008 using a random cluster sampling design of infectious disease hospitals in seven high HIV-prevalent provinces (municipalities). Univariate analysis and logistic regression were used to study the determinants of HIV and HBV and/or HCV co-infection. The overall prevalence was 41·83% (95% CI 40·36–43·30) for anti-HCV and 12·49% (95% CI 11·50–13·48) for HBsAg, respectively. The prevalence of anti-HCV and HBsAg varied according to the route of HIV transmission. Compared to those with sexually acquired HIV infection, intravenous drug users and blood donors/recipients had the greatest risk of carrying anti-HCV. Needle sharing and unprotected sexual exposures are important modes of transmission for HBV. Further interventions including health education and harm reduction strategies should be implemented in high-risk populations.

Key words: Hepatitis B virus, hepatitis C virus, HIV, prevalence.

INTRODUCTION

Chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection is common in patients infected with the human immunodeficiency virus (HIV), due to the common risk factors for transmission. Since the decline in HIV-related morbidity and mortality after the

introduction of highly active antiretroviral therapy (HAART), liver disease caused by chronic infection with HBV or HCV has become an increasingly important cause of morbidity and mortality in HIV-infected patients [1]. Despite the initially mild clinical course, the HBV/HCV-related liver disease in HIV-infected patients is more progressive, including the development of cirrhosis and hepatocellular carcinoma (HCC), compared to patients with HBV/HCV infection only and thus contributes significantly to the morbidity and mortality of HIV-infected patients [2].

Hepatitis B is endemic in China, where a national survey in 2002 showed a 9% rate of HBsAg in the

* Author for correspondence: Dr Hao Wu, STD and AIDS Clinical Center, Beijing Youan Hospital, Capital Medical University, No. 8 Xitoutiao, You An Men, Beijing 100069, P.R. China.

(Email: wuccmu2010@163.com)

† These authors contributed equally to this work.



Fig. 1. Map of cumulative cases of HIV infection in China according to province by the end of 2008. Sample sites are indicated by black dots (data from Chinese CDC).

general population [3]. In 2002, China integrated hepatitis B vaccine into the National Expanded Programme on Immunization (EPI), with emphasis on providing a timely birth dose (within 24 h of birth). A recent epidemiological serosurvey of hepatitis B in China found that the weighted prevalence of HBsAg for the Chinese population aged 1–59 years was 7.2%, and in children aged <5 years it was only 1.0% [4]. Although prevalence of HBsAg has declined as a result of the effectiveness of the vaccination programme, HBV infection is still endemic in China. According to a multicentre epidemiological study in China between 1991 and 1995 (about 90 000 persons investigated), HCV prevalence averaged 2.2% in the general population (range 0.52–3.15% between participating centres), amounting to about 26.4 million infected individuals [5]. Recent social and economic changes greatly increase the potential for a substantial Chinese HIV epidemic. By 2007, the number of people living with HIV is estimated to be 700 000, including 85 000 AIDS patients [6]. Limited data have shown that HCV and HBV infection in HIV-positive patients was more prevalent than in the general population.

In this study, a multicentre epidemiological survey was conducted to examine the situation of co-infection of HIV, HCV and/or HBV in different populations in China according to the route of transmission in seven high HIV-prevalent provinces (municipalities).

PATIENTS AND METHODS

The study was carried out from May 2007 to September 2008 in the infectious disease hospitals in seven high HIV-prevalent provinces (municipalities) with consideration of the main mode of HIV transmission in each region: Yunnan, Xinjiang and Sichuan (intravenous drug use); Guangdong and Beijing (sexual contact); Henan and Shanxi (blood transmission and mother–child transmission). In each province, 1–3 cities where free antiretroviral therapies are available were selected for cluster sampling: Xichang (Sichuan province); Yining (Xinjiang province); Dehong, Dali (Yunnan province); Guangzhou (Guangdong province); Choy, Zhoukou, Nanyang (Henan province); Linfen, Yuncheng (Shanxi province); and Beijing and surrounding areas. The sample sites were marked on a map with cumulative cases of HIV infection in China according to province by the end of 2008 (Fig. 1). The study population comprised all the HIV-positive patients who were recruited or followed up at least once at the Department of (STD and) AIDS with informed consent during the study period. Demographic information and details regarding risk factors for infection such as intravenous drug use, sexual contacts, commercial blood (plasma) donation, blood transfusion, mother–child transmission and major or minor surgical or dental operations were collected.

Table 1. Number (%) of patients with anti-HCV or/and HBsAg according to route of transmission of HIV

Transmission category	No of patients (%)	Anti-HCV	HBsAg	Hepatitis B and C co-infection
Men who have sex with men	618 (14.4)	24 (3.9)	72 (11.7)	4 (0.5)
Heterosexuals	1102 (25.6)	91 (8.3)	159 (14.4)	19 (1.7)
Blood donors/recipients	1153 (26.8)	797 (69.1)	96 (8.3)	43 (3.7)
Intravenous drug users	1079 (25.1)	847 (78.5)	190 (17.6)	156 (14.5)
Mother-child transmission	154 (3.6)	12 (7.8)	7 (4.5)	0 (0.0)
Other/unknown	200 (4.6)	30 (14.9)	14 (7.0)	3 (1.5)
Total	4306 (100.0)	1801 (41.8)	538 (12.5)	225 (5.23)

Presence of anti-HIV antibodies was determined by enzyme-linked immunosorbent assay (ELISA) screen (Organon Teknika Corporation, The Netherlands). All positive tests were retested in duplicate and confirmed by Western blot assay (Genelabs Diagnostics, Singapore). HBsAg and anti-HCV were identified by ELISA according to the manufacturer's instructions, using kits from Biokit, Solin (Italy) for HBsAg and Wantai Biopharm (Beijing) for anti-HCV. All the positive samples were retested by the same method. HBsAg and anti-HCV were confirmed by two positive tests.

The χ^2 test was used to compare percentages and Student's *t* test to compare means. Prevalence estimates are presented with their 95% confidence interval. We used univariate analysis and logistic regression to study the determinants of anti-HCV carriage, with route of HIV transmission and presence or absence of HBsAg as explanatory variables and sex as a stratifying variable. The same analyses were performed for HBsAg, taking route of HIV transmission and presence or absence of anti-HCV as determinants and sex as a stratifying variable. In the multivariate analyses, age was adjusted and HIV transmission categories were coded with an indicator (dummy) variable. For men, men who have sex with men (MSM) was the reference category, and men who reported both homosexual contacts and intravenous drug use were classified as intravenous drug users (IDUs). For women, heterosexuals served as the reference category.

RESULTS

Characteristics of participants

Over 17 months, 4306 HIV-positive patients were enrolled in the study, with median (range) age of 36 (0.8–85) years and mean (s.d.) age 36.2 (10.8) years. The sample included more male patients (71.3%)

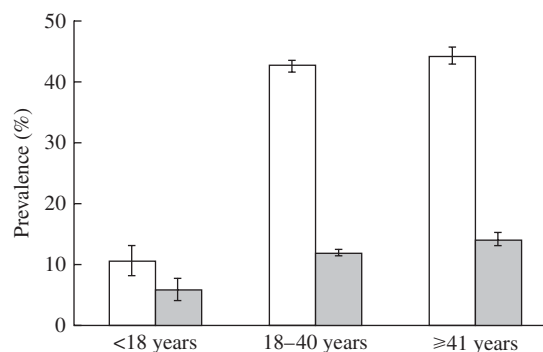


Fig. 2. Prevalence ($p \pm S_p$) of anti-HCV (□) and HBsAg (■) by age in HIV-positive Chinese patients.

than women (28.7%). In total, 43.71% of the patients were farmers and 20.2% were unemployed. Of the 168 patients aged ≤ 14 years, 62.5% were boys and 37.5% were girls.

The prevalence of HIV and HBV or HCV co-infection

The serological status for both HBV and HCV was positive for 225 of the 4306 patients (5.2%, 95% CI 4.6–5.9, Table 1). Of the remaining 4081, 1576 had been tested positive for only hepatitis C, 313 for only hepatitis B, and 2192 for neither. The overall prevalence of HIV and HBV or HCV co-infection in patients tested in this population was 49.1% (95% CI 47.6–50.6). More specifically, the overall prevalence of anti-HCV was 41.8% (95% CI 40.4–43.3). The overall prevalence of HBsAg was 12.5% (11.5–13.5%). Patients who were co-infected with either of the hepatitis viruses and HIV were older ($P < 0.05$) compared to those who were not co-infected (Fig. 2).

Determinants of presence of anti-HCV

In the univariate analysis the prevalence of anti-HCV varied according to the route of HIV transmission

Table 2. *Determinants of anti-HCV carriage according to sex**

	Prevalence of anti-HCV (%)	OR (95% CI)	P value
Men (n = 3241)			
HIV transmission category			
Men who have sex with men	3.9	Reference	
Heterosexuals	9.7	2.9 (1.7–4.7)	<0.001
Blood donors/recipients	75.0	68.0 (43.4–106.6)	<0.001
Intravenous drug users	76.9	83.9 (54.3–129.6)	<0.001
Mother–child transmission	8.7	2.4 (1.1–5.3)	0.021
Other/unknown	13.9	4.8 (2.5–9.4)	<0.001
HBsAg			
Negative	45.3	Reference	
Positive	42.2	0.9 (0.7–1.2)	0.39
Women (n = 1065)			
HIV transmission category			
Heterosexuals	6.4	Reference	
Blood donors/recipients	55.7	17.1 (11.1–26.3)	<0.001
Intravenous drug users	92.8	253.4 (103.5–620.6)	<0.001
Mother–child transmission	6.5	1.3 (0.5–3.3)	0.63
Other/unknown	16.9	3.2 (1.5–6.6)	0.002
HBsAg			
Negative	31.8	Reference	
Positive	34.7	1.0 (0.6–1.9)	0.92

* Logistic regression analysis.

($P < 0.001$, Table 1). The prevalence of anti-HCV was 11.01 times higher in those with bloodborne (needle sharing and blood donation/transfusion) HIV infection (1644/2232, 73.7%) than in those with sexually acquired HIV infection (115/1720, 6.7%), and 8.87 times higher than those with mother–child transmitted HIV infection (12/154, 7.8%).

The crude prevalence of anti-HCV was higher in men than women (45.0% vs. 32.3%, $P < 0.001$). The crude prevalence of anti-HCV was not significantly different between patients with HBsAg and those without (40.3% vs. 42.0%, $P = 0.46$).

In men, the prevalence of anti-HCV differed according to HIV transmission category (Table 2). Compared to homosexuals, IDUs had a greater risk of carrying anti-HCV (OR 83.9), as did those who had blood donation/transfusion (OR 68.0). Mother–child transmitted patients had a higher risk of carrying HBsAg than homosexuals (OR 2.4). For women, the prevalence of anti-HCV was also associated with bloodborne HIV transmission. Compared to heterosexuals, female IDUs had the highest risk of carrying antibodies to HCV (OR 253.4), followed by blood donors/recipients (OR 17.1). In mother–child transmitted patients, the prevalence of anti-HCV in boys (8/92) and in girls (4/62) were not significantly

different ($P = 0.61$). No relation was observed between anti-HCV and presence of HBsAg ($P > 0.05$) in both men and women.

Determinants of the prevalence of HBsAg

In the univariate analysis the prevalence of HBsAg varied with HIV transmission category ($P < 0.001$, Table 1). The prevalence of HBsAg in those with bloodborne HIV infection (286/2232, 12.8%) was similar to those with sexually acquired HIV infection (231/1720, 13.4%). There was no significant difference in the prevalence of HBsAg between men and women (12.0% vs. 13.9%, $P = 0.23$), and between patients with anti-HCV and those without (12.5% vs. 12.4%, $P = 0.26$).

Table 3 shows the multivariate analysis stratified by sex. For men, heterosexuals and IDUs had a higher risk of carrying HBsAg than MSM ($P < 0.05$). The prevalence of HBsAg in blood donors/recipients was not significantly different with that in MSM ($P = 0.19$). For women, IDUs had a higher risk of carrying HBsAg than heterosexuals ($P = 0.02$). However, blood donors/recipients had a lower risk of carrying HBsAg than heterosexuals ($P = 0.04$). In the mother–child transmitted patients, the prevalence of HBsAg in boys

Table 3. *Determinants of HBsAg carriage according to sex**

	Prevalence of HBsAg (%)	OR (95% CI)	<i>P</i> value
Men (<i>n</i> = 3241)			
HIV transmission category			
Men who have sex with men	11.6	Reference	
Heterosexuals	16.3	1.4 (1.0–1.9)	0.041
Blood donors/recipients	8.7	0.8 (0.5–1.2)	0.19
Intravenous drug users	17.3	1.7 (1.2–2.5)	0.002
Mother–child transmission	3.3	0.3 (0.1–0.8)	0.020
Other/unknown	6.2	0.5 (0.2–1.1)	0.067
Anti-HCV			
Negative	12.6	Reference	
Positive	11.4	0.9 (0.7–1.2)	0.39
Women (<i>n</i> = 1065)			
HIV transmission category			
Heterosexuals	11.9	Reference	
Blood donors/recipients	7.4	0.6 (0.4–1.0)	0.039
Intravenous drug users	19.8	2.2 (1.1–4.8)	0.018
Mother–child transmission	6.5	0.4 (0.2–1.3)	0.19
Other/unknown	8.5	0.7 (0.3–1.7)	0.43
Anti-HCV			
Negative	13.3	Reference	
Positive	14.9	1.0 (0.6–1.8)	0.98

* Logistic regression analysis.

(3/92) and in girls (4/62) were not significantly different ($P=0.59$). There was no difference between presence of anti-HCV and HBsAg in both men and women ($P>0.05$).

DISCUSSION

Our study of a large sample of patients infected with HIV allowed us to estimate precisely the prevalence of the serological markers of hepatitis C and B infections. We used a random cluster sampling design of infectious disease hospitals in seven high HIV-prevalent provinces. Although HIV has been reported in all 31 Chinese provinces, autonomous regions, and municipalities, about three quarters of infected persons resided in these seven provinces. The Chinese government requires county-level jurisdictions to provide free antiretroviral drugs to the poorer citizens who need treatment [7]. The percentage of transmission routes of our sample is similar to that of the cumulative reported cases of HIV infectious by the end of 2008 in China [8]. These factors suggest that our sample was representative of the population of patients infected with HIV.

Our estimate of the overall prevalence of anti-HCV is 41.83%, and for HBsAg it is 12.49% in

HIV-positive Chinese patients. Because of shared routes of transmission, co-infection with either HBV or HCV is common in HIV-infected patients, and the prevalence of both is higher than in the general Chinese population. We also found that the prevalence of anti-HCV and HBsAg varied with route of HIV transmission.

The prevalence of anti-HCV is different from that reported in previous studies: a prevalence of 16.1% ($n=1687$) in USA [9], 42.5% ($n=1935$) in France [10], 13.8% ($n=181$) in Greece [11], and 5.23% ($n=172$) in Malawi [12]. The reason for these differences may be that the distribution of HIV transmission categories varies in the different studies.

HCV is predominantly found in persons who have had large or repeated percutaneous exposures to infectious blood, such as persons receiving unfiltered blood or untreated clotting factor products, and IDUs [13]. The present study showed that IDUs were 11.73 times more likely to be infected with HCV than those with sexually acquired HIV infection. A recent meta-analysis showed that the pooled prevalence of HCV infection in IDUs in China was 61.4% (95% CI 55.7–67.2) [14]. Data from China's 2005 sentinel surveys indicate that 46.8% of IDUs have reported sharing syringes, a dramatic increase from the rate in

2004, which was 38.6% [15]. Most of female drug users engaged in the sex trade due to economic pressure from their drug use behaviours. This may be the reason that the prevalence of anti-HCV in female IDUs is higher than that in male IDUs.

In our study, the prevalence of HIV and HCV co-infection was also high (69.12%) in the HIV-positive blood donors/recipients. Due to non-standard paid blood donation between 1990 and 1997, many blood donors became infected with HIV/HCV/HBV in villages in central China. The method of single-collect plasma used greatly increases the risk of infection [1, 16]. Since 1993, blood donors have been required to be screened for anti-HCV, the channel of HCV infection transmitted by blood/plasma collection and as a result blood transfusion has been effectively controlled. However, in many infertile areas, the measure has not been fully implemented, which has caused many HIV-infected patients to also be infected with HCV.

HCV is not efficiently transmitted by sexual or perinatal exposures, which are important modes of transmission for HBV and HIV. Although IDUs and former blood/plasma donors account for the majority of the infected, heterosexual intercourse has recently become the primary mode of HIV transmission in China [17–19]. Being poorly educated and afraid of being arrested, female sex workers are vulnerable to HIV infection and other communicable diseases and are difficult to target for prevention strategies [20]. These are the reasons why prevalence of HCV in heterosexuals is significantly higher than that in the general population.

In HIV-positive persons studied from Western Europe and the USA, chronic HBV infection has been found in 6–14% overall [21–23], including 4–6% of HIV-positive heterosexuals, 9–17% of HIV-positive homosexuals, and 7–10% of IDUs. In our study, sexual and injection drug use exposures accounted for most HBV and HIV co-infections. Conventional screening for HBV in blood donors and effective vaccine and immunoglobulin against HBV contribute to the low HBV co-infection rate in those HIV-positive patients infected by blood transfusion and mother–child transmission. Recently, Shang *et al.* reported that mini-pool nucleic acid testing (NAT) identified two HBV DNA + blood donors in a sample of 41 301 donations negative for HBsAg, anti-HCV, anti-HIV, syphilis (anti-treponemal antibody) and with normal alanine transaminase in Shenzhen, China [24]. HBV NAT has now been implemented in

some countries. The potential for HBV DNA screening to improve the detection of HBV infection is important as HBV infection is still endemic in China.

The mother–child transmission of HIV now accounts for 1.1% of people living with HIV in China [8]. From 2004, plans to reduce HIV infection by mother–child transmission have been implemented [25, 26]. It will probably not be a main route of HIV infection in the future in China. The prevalence of anti-HCV and HBsAg in these children is higher than that in general population of the same age [4, 5].

The number of people with HIV infection is increasing in China. Although the prevalence of HCV/ HBV varied in different populations infected with HIV through different routes, IDUs, blood donors/recipients and commercial sex workers are all at highest risk of co-infection. Future efforts should focus on changing risk behaviours, including harm reduction and condom promotion. For example, the government is working with neighbouring countries to prevent drug smuggling, and is increasing anti-drug education for the general population and in schools [27]. Harm reduction strategies, such as methadone maintenance treatment and needle exchange programmes, should be implemented.

The average usage rate of condoms in commercial sex workers is 30% [28]. Use of condoms depends on the customer [20]. Some safe-sex education should be introduced in order to increase the use of condoms by promoting the self-esteem of the sex workers and improving their negotiating skills. Free condoms should also be provided in all hotel rooms.

In China the HCV infection rate in HCV seronegative blood donors aged between 18 and 60 years is around 0.08%, higher than that of 0.041% reported in Western countries [29, 30]. Considering the large population of blood donors in China, the risk of HCV transmission via blood transfusion is still significant, although HCV antibody testing has been used. Therefore, to reduce the residual risk of HCV infection post-transfusion, we strongly recommend testing for HCV RNA or/and HCV core antigen as an essential screening for blood donors who are negative for anti-HCV.

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DECLARATION OF INTEREST

None.

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