

HIV, HCV, and HBV Co-Infections in a Rural Area of Shanxi Province with a History of Commercial Blood Donation*

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Abstract

Background: Unhygienic blood collection in the early 1990s led to blood-borne infections in Central China. This study aimed to estimate human immunodeficiency virus (HIV) co-infection with hepatitis C and B viruses (HCV and HBV) and their risk factors in a rural area of Shanxi Province with a history of commercial blood donation.

Methods: A cross-sectional study was conducted in 2004. All adult residents in the target area were invited to participate in the study. Face-to-face interviews were completed and blood specimens were tested for HIV, HCV, and HBV surface antigen (HBsAg).

Results: Prevalence rates of HIV, HCV, and HBsAg were 1.3% (40/3 062), 12.7% (389/3 062), and 3.5% (103/2982), respectively. Of the 40 HIV-positive specimens, 85% were HCV positive and 2.5% were HBsAg positive. The history of commercial blood donation was positively associated with HIV, HCV, and HIV/HCV co-infections, but was negatively associated with HBsAg seropositivity. Migration for employment in the last 5 years was positively related to HIV, HBsAg, and HIV/HCV co-infections. Univariate logistic analysis showed that illegal drug use, number of sex partners, extramarital sex behavior, commercial sex behavior, and condom use rate were not related to anti-HIV, anti-HCV, HBsAg seropositivity or their co-infections.

Conclusion: The history of commercial blood donation was the main risk factor for HIV, HCV, and HIV/HCV co-infections in this former commercial blood donation area. HIV and HCV prevention and treatment interventions are important in this area.

Key words: Human immunodeficiency Virus; Co-infections; Hepatitis C Virus; Hepatitis B Virus Surface Antigen; Commercial Blood Donation

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INTRODUCTION

Since the first case of AIDS in China was diagnosed in 1985^[1], the HIV/AIDS epidemic has undergone three stages in this country: the entry and sporadic stage, the localized spread stage, and the generally disseminated stage. Collection of unhygienic plasma/blood donations in rural areas of China during the mid-1990s led to regional HIV epidemics and marked the start of the generally disseminated stage^[2]. During this period, blood was collected from multiple paid donors, plasma was separated, and red blood cells, which were often mixed with those from other donors, were re-infused to allow more frequent donations. These illegal practices set the stage for contamination of the commercial-source plasma/blood supply and quick spread of blood-borne diseases such as HIV, hepatitis C (HCV), and hepatitis B (HBV)^[3].

The 2005 estimate indicated that 10.7% of all HIV infections were related to former commercial plasma/blood donation, affecting recipients of blood or blood products through transfusions in China^[4]. While HIV infection in former plasma/blood donors (FPDs) has been well-documented and has elicited a strong government response (e.g., China CARES program and "Four Frees and One Care" policy), less attention has been given to its co-infection with other blood-borne diseases, such as HCV and HBV. Investigation of co-infection with HCV and HBV is crucial because co-infection with HIV accelerates disease progression in both HCV and HBV infected individuals^[5], and patients with HIV and viral hepatitis have a greater liver mortality than do patients with only HIV^[6]. In addition, HIV prevalence in China's general population is still relatively low (0.05% in 2005)^[4], but 3.2% of the general population is infected with HCV and 9.8% are HBV carriers (HBsAg positive)^[7]. The spread of HCV and HBV and co-infection with HIV is possibly a greater public health threat in China. Several risk factors for HIV and HCV in FPDs have been identified in previous studies, including plasma/blood donation, middle age, frequency of plasma donation, different settings of plasma/blood donation station, having a HIV-or HCV-infected partner, and multiple sex partners^[3,8-10], but less is known about risk factors for HBV infection in FPDs.

Illegal and unhygienic blood collection has been prohibited in China since the "Law of Blood Donation" was promulgated in 1998^[11], and it is thus less directly related to new HIV/AIDS cases in China.

Still, HIV-infected FPDs may have an impact on secondary HIV transmission to other populations through sexual networks and drug use. China's economic reforms in the 1980s allowed and encouraged population mobility, and as in other countries worldwide^[12], migration has had a major influence on China's current HIV epidemic^[13]. Some studies have reported higher HIV and STI rates in migrant male laborers^[14], possibly due to changes in sexual behaviors and drug use to cope with social isolation^[15]. However, the relationship between migration and HIV infection has been inconsistent among China's FPD populations^[8,16]. The objectives of our study, therefore, were to identify the prevalence of HIV co-infection with HCV and HBV and the associated risk factors, including migration, in rural Shanxi province, a former commercial plasma/blood donation area.

METHODS

Study Design, Site, and Population

A cross-sectional study among FPDs was conducted from May to August 2004. A county in southern Shanxi Province was chosen as our study site. The city area to which our study site belongs had reported 414 HIV cases as of December 2003, accounting for 64.3% of all cases reported in this province^[17]. A pilot study conducted from November to December 2003 found that the prevalence rates of HIV, HCV, and syphilis were 1.3%, 8.2%, and 0, respectively, among adult villagers^[18-19]. After this pilot study, the four villages with the highest HIV prevalence and relatively high numbers of plasma/blood donors were chosen for the cross-sectional study. All villagers were invited to participate if they were 1) 18-64 years old, 2) living in these villages for more than six months, and 3) capable and willing to provide informed consent and contact information. Written informed consent from each of the participants was obtained before the collection of any personal information.

Data Collection

All participants were asked to administer a standardized questionnaire by same-sex interviewers to collect socio-demographic information, medical history, history of commercial plasma/blood donation, history of sexual behaviors, and history of drug use.

A venous blood specimen was collected and

plasma was centrifuged for HIV, HCV antibody, and HBV surface antigen (HBsAg). HIV antibody was screened by an enzyme-linked immunosorbent assay (ELISA) (Organon Teknika, Boxtel, Co, Ltd, Netherlands) and confirmed by a Western blot assay (HIV Blot 2.2 WB; Genelabs Diagnostics, Singapore)^[20]. ELISA was used to test HCV antibody (GBI Biotech Co., Ltd, Beijing, China) and HBsAg (Kinghamk Co., Ltd, Beijing, China).

Statistical Analysis

Data were analyzed by using SAS 9.1 software (SAS Institute Inc., Cary, NC, USA). Point prevalence rates of HIV, HCV, HbsAg, and their co-infections were calculated. Univariate logistic analyses were conducted to identify socio-demographic characteristics and risk factors associated with HIV, HCV, and HBsAg seropositivity, and all variables with statistical significance ($P < 0.05$) were entered into multivariate logistic regression analysis in a step-wise manner to screen relevant variables.

Quality Control and Ethical Issues

The protocol of this study was approved by the institutional review boards of the National Center for AIDS/STD Prevention & Control (NCAIDS), NIH, and China Centers for Disease Control and Prevention (CDC) to assure the quality of the study and protection of participants' rights. All the staff received relevant training before the study. Laboratories involved were approved by the national reference laboratory, NCAIDS, China CDC, and the AIDS laboratory at the Shanxi Provincial CDC. All the laboratory operations were processed according to the manufacturers' instructions or the protocols that had been confirmed by the laboratory experts of NIH.

RESULTS

Participant Recruitment and Characteristics

Of the 3 718 villagers aged 18-64 years in the four villages, 82.4% (3 062/3 718) completed questionnaires and provided blood specimens. Eighty specimens were not tested for HBsAg because of refusals of the participants. There was no significant difference in age, sex, education level, marital status, occupation, migration status, history of plasma/blood donation, and number of sex partners between those tested and those not tested for HBsAg ($P > 0.05$).

HIV, HCV, and HBsAg Prevalence

HIV, HCV, and HBsAg prevalence rates were 1.3% (40/3 062), 12.7% (389/3 062), and 3.5% (103/2 982), respectively. One participant was positive for HIV, HCV, and HBsAg. Of the 40 HIV-seropositive participants, 85% (34/40) were co-infected with HCV; one of the 40 participants was HBsAg seropositive. Of the 389 HCV-seropositive participants, 2.57% (10/389) were HBsAg seropositive. Of the 103 HBsAg-positive participants, 10 were co-infected with HCV.

Factors Associated with HIV, HCV, and HBsAg Seropositivity and Their Co-Infections

In univariate analyses, HIV was significantly associated with a history of ever plasma donation (OR, 85.4; 95% CI, 25.7-283.8), a history of whole blood donation only (OR, 11.2; 95% CI, 3.1-40.9), primary school education or below (OR, 3.7; 95% CI, 2.0-7.0), living in a village with an illegal plasma collection station (OR, 3.1; 95% CI, 1.7-5.9), and migration for labor in the last 5 years (OR, 2.0; 95% CI, 1.1-3.7). HCV was significantly associated with a history of ever plasma donation (OR, 35.3; 95% CI, 25.5-48.8), a history of whole blood donation only (OR, 4.9; 95% CI, 3.7-6.5), being male (OR, 1.4; 95% CI, 1.1-1.7), older than 30 years of age (OR, 13.4; 95% CI, 6.6-27.1), primary school education or below (OR, 1.9; 95% CI, 1.5-2.4), living in a village with an illegal plasma collection station (OR, 3.1; 95% CI, 2.5-3.9), a history of dental care (OR, 1.4; 95% CI, 1.1-1.8), bleeding at haircut (OR, 1.8; 95% CI, 1.2-2.7), being divorced or widowed (OR, 6.1; 95% CI, 2.2-16.9), and farming income only (OR:1.3, 95% CI:1.0-1.6). HBsAg carriage was negatively associated with a history of ever plasma donation (OR, 0.4; 95% CI, 0.1-1.0), a history of whole blood donation only (OR, 0.2; 95% CI, 0.1-0.5), and older than 30 years of age (OR, 0.5; 95% CI, 0.3-0.8). By contrast, being male (OR, 1.5; 95% CI, 1.0-2.3) and migration for labor in the last 5 years (OR, 1.7; 95% CI, 1.1-2.5) were positively associated with HBsAg carriage. Being male (OR, 2.4; 95% CI, 1.2-5.1), migration for labor in the last 5 years (OR, 2.4; 95% CI, 1.2-4.8), primary school education or below (OR, 3.1; 95% CI, 1.6-6.1), and living in a village with an illegal plasma collection station (OR, 3.0; 95% CI, 1.5-5.9) were significantly associated with HIV/HCV co-infections. All HIV/HCV co-infected participants were FPDs and older than 30 years of age. A history of ever plasma donation (OR, 5.0; 95% CI, 1.2-21.1) and primary

school education or below (OR, 3.6; 95% CI, 1.0-12.8) were positively associated with HCV/HBV co-infection; all HIV-infected and HCV/HBV-co-infected participants were older than 30 years of age. HIV/HBV co-infection was not analyzed in univariate analyses because only

one participant was HIV/HBV positive (Table 1). A history of blood transfusion, illegal drug use, unsafe sex, and condom use were not significantly associated with HIV, HCV, HBsAg seropositivity, or with HIV/HCV, HCV/HBV co-infection.

Table 1. Univariate Analysis of Factors Associated with HIV, HCV, HBV Infection and HIV/HCV, HCV/HBV Co-infection

Variables	HIV		HCV		HBsAg		HIV/HCV		HCV/HBsAg	
	Positive rate (%)	OR(95% CI)	Positive rate (%)	OR(95% CI)	Positive rate (%)	OR(95% CI)	Positive rate (%)	OR(95% CI)	Positive rate (%)	OR(95% CI)
History of Blood/Plasma Donation										
None	0.14		4.68		4.39		0		0.24	
Ever Plasma Donation	10.63	85.4(25.7-283.8)*	63.39	35.3(25.5-48.8)*	1.58	0.4(0.1-1.0)*	9.84	-	1.19	5.0(1.2-21.1)*
Whole Blood Donation only	1.54	11.2(3.1-40.9)*	19.54	4.9(3.7-6.5)*	1.10	0.2(0.1-0.5)*	1.38	-	0.32	1.3(0.3-6.8)
Gender										
Female	0.91		10.9		2.76		0.65		0.54	
Male	1.70	1.9(1.0-3.6)	14.51	1.4(1.1-1.7)*	4.14	1.5(1.0-2.3)*	1.57	2.4(1.2-5.1)*	0.13	0.2(0.1-1.2)
Age(years)										
<=30	0		1.35		5.57		0		0	
>30	1.62	-	15.44	13.4(6.6-27.1)*	2.95	0.5(0.3-0.8)*	1.38	-	0.42	-
Primary School Education or Below										
No	0.74		10.43		3.71		0.69		0.19	
Yes	2.68	3.7(2.0-7.0)*	18.19	1.9(1.5-2.4)*	2.85	0.8(0.5-1.2)	2.12	3.1(1.6-6.1)*	0.68	3.6(1.0-12.8)*
Living in a Village with a Illegal Blood Collection Station										
No	0.78		8.25		3.48		0.68		0.20	
Yes	2.40	3.1(1.7-5.9)*	21.88	3.1(2.5-3.9)*	3.40	1.0(0.6-1.5)	2.00	3.0(1.5-5.9)*	0.62	3.1(0.9-11.1)
Migrating for Labor in Last 5 Years										
No	1.02		12.28		2.90		0.78		0.38	
Yes	2.01	2.0(1.1-3.7)*	13.73	1.1(0.9-1.4)	4.79	1.7(1.1-2.5)*	1.90	2.4(1.2-4.8)*	0.23	0.6(0.1-2.8)

Note. History of dental dental care , bleeding at haircut , divorced or widowed and farming income only were also positively associated with HCV infection. $P < 0.05$.

In multivariate analyses, HIV infection was independently associated with a history of plasma donation (OR, 70.6; 95% CI, 20.8-239.1), a history of whole blood donation only (OR, 11.1; 95% CI, 3.0-41.1), primary school education or below (OR, 2.2; 95% CI, 1.1-4.3), and migration for labor in the last 5 years (OR, 2.5; 95% CI, 1.2-4.8). HCV infection was independently associated with a history of plasma donation (OR, 22.8; 95% CI, 16.3-32.0), a history of whole blood donation only (OR, 3.1; 95% CI, 2.3-4.2),

living in a village with an illegal plasma collection station (OR, 2.2; 95% CI, 1.7-2.9), older than 30 years of age (OR, 5.1; 95% CI, 2.5-10.7), and being male (OR, 1.5; 95% CI, 1.2-1.9). HBsAg seropositivity was negatively associated with a history of ever plasma collection (OR, 0.4; 95% CI: 0.1-1.0) and a history of whole blood donation only (OR, 0.3; 95% CI, 0.1-0.5), but it was positively associated with migration for labor in the last 5 years (OR, 1.6; 95% CI, 1.1-2.4). HIV/HCV co-infection was independently associated

with living in a village with an illegal plasma collection station (OR, 2.6; 95% CI, 1.3-5.3), being male (OR, 2.4; 95% CI, 1.1-5.5), and primary school education or below (OR, 3.9; 95% CI, 1.9-7.9); it was

marginally associated with migration for labor in the last 5 years (OR, 2.1; 95% CI, 1.0-4.4). Independently, HCV/HBV co-infection was associated only with primary school education or below (Table 2).

Table 2. Multivariate Analyses for Factors Associated with HIV, HCV, HBV Infection and HIV/HCV, HCV/HBV Co-infection

Testing results	variable	Adjusted OR(95% CI)	P
HIV Positive	History of plasma donation	70.6(20.8-239.1)	<0.0001
	History of whole blood donation only	11.1(3.0-41.1)	0.0003
	Primary school education or below	2.2(1.1-4.3)	0.0274
	migrating for labor in last 5 years	2.5(1.2-4.8)	0.0098
HCV Positive	History of plasma donation	22.8(16.3-32.0)	<0.0001
	History of whole blood donation only	3.1(2.3-4.2)	<0.0001
	Living in a village with a illegal blood collection station	2.2(1.7-2.9)	<0.0001
	Age(>30years)	5.1(2.5-10.7)	<0.0001
	Male	1.5(1.2-1.9)	0.0007
HbsAg Positive	Income from farming only	1.3(0.9-1.6)	0.0779
	History of plasma donation	0.4(0.1-1.0)	0.0424
	History of whole blood donation only	0.3(0.1-0.5)	0.0005
HIV/HCV	migrating for labor in last 5 years	1.6(1.1-2.4)	0.0233
	Living in a village with a illegal blood collection station	2.6(1.3-5.3)	0.0066
	Male	2.4(1.1-5.5)	0.0310
	Primary school education or below	3.9(1.9-7.9)	0.0002
HCV/HBsAg	migrating for labor in last 5 years	2.1 (1.0-4.4)	0.0510
	Primary school education or below	3.6(1.0-12.8)	0.0470

Risk Behaviors

Of the 3 062 participants, 1.37% had a history of blood transfusion, and 0.39% had a history of illegal drug use. Of the 2 953 married participants, 196 (6.64%) had a history of extramarital sex, among whom 162 (82.65%) reported never using a condom. Almost 1% (27/3 062) reported a history of engaging in commercial sex, and 48.15% of these 27 reported never using a condom.

DISCUSSION

Our study showed that the prevalence rates of HIV (1.3%) and HCV (12.7%) in this area of southern Shanxi Province were much higher than their overall prevalence rates in China (0.05% for HIV⁴ and 3.2% for HCV⁷), but the HBsAg rate in our study was much lower than the nationwide one (HBsAg carriage rate 9.8%⁷). Compared with other highly-affected FPD

communities^[8,10,16], however, HIV prevalence was lower, mainly due to the relatively late introduction of HIV into our study communities. This situation in rural Shanxi Province has been discussed in detail elsewhere^[21]. Prevalence of HIV/HCV co-infection has been reported to range from 68.4% to 87.3%^[16, 22-23] among HIV-positive FPDs, with a much lower HBsAg seropositive rate, reportedly between 3.9% and 4.8%^[22-23]. This pattern is consistent with the proportionately high rates of HIV, HCV, and their co-infection and low rates of HBV and co-infection with HIV in our study.

HIV, HCV, and their co-infections were all independently associated with a history of plasma donation and a history of whole blood donation, but HBsAg positivity was not associated with these factors. Blood screening regulations may account for this discrepancy, considering the fact that screening for HBV has been routinely practiced since the 1980s, but screenings for HIV and HCV were not available

until 1993. In addition, the low prevalence of HBsAg in the general population of our study area may help explain this finding; for instance, another study in Shanxi Province has found a relatively low HBsAg prevalence rate (5.8%) among non-FPDs^[24].

Migration for employment in the last 5 years was independently associated with HIV, HIV/HCV, and HBsAg seropositivities, yet due to the cross-sectional nature of this study the exact relationship with migration is unclear. Several risky behaviors such as unprotected sex and drug use have been associated with the migrant population in China, likely stemming from social isolation^[15,25]. Some studies in China have also found an increased number of STIs in this population^[14,26], though others have reported low STI and HIV rates^[27-28]. In our study, drug use, unsafe sex, and condom use were not associated with HIV, HCV, or HBV. It has been proposed that males migrating for employment are more often young, poor, and unmarried^[25]. Such men may have been more likely to engage in risky practices such as unsafe paid blood donation, especially in villages where commercial blood donation sites were readily accessible. It is also possible that they were already infected in nearby villages with illegal donation practices and later migrated for employment due to their HIV status. Perhaps, it is more important that those who migrated in the past may be predisposed to continuing migrant labor. Although these FPDs are no longer likely to be selling blood products as a result of new regulations and reports of low illegal drug use (0.88%), problems remain as the rates of extramarital sex and commercial sex are high and condom use rates are low. Migrant FPDs infected with HIV, HCV, or HBV may therefore be at risk for unsafe sex practices and subsequently spread these infections to high-risk populations such as sex workers and to the general population through their regular partners. For example, although an earlier study of FPDs in Anhui Province found that HIV was not transmitted sexually^[3], a recent study in Anhui reported evidence of sexually transmitted HIV to non-FPDs^[10].

Histories of dental therapy and bleeding during haircut were also associated with HCV in the univariate analysis and may therefore represent another mechanism for infection. This finding underscores the need to continue education about preventing blood-borne disease transmission in less conventional settings such as dental offices and public venues such as hairdressing salons.

This study had three notable limitations. First, our study was conducted in an area where illegal blood collection practices had been widespread ten years ago, and so an unknown number of HIV-infected participants might have already died, a possibility that could lead to an underestimation of HIV prevalence. Second, our study sites were chosen from relatively high rates of HIV infection and plasma/blood donation, and so the results may reflect the highest levels of HIV and HCV infections in this area. Third, our study tested only HCV antibody and HBsAg, and so HCV-infected patients with negative HCV antibodies but with positive HCV RNA might have been missed. Similarly, HBsAg possibly failed to include all participants who were once infected with HBV.

In summary, our study found that HIV and HCV and their co-infection were mainly caused by unhygienic blood collection, and prevention and treatment interventions should focus on both HIV and viral hepatitis in the former plasma/blood donation communities of Shanxi Province. Community members, especially migrant laborers, should receive appropriate education on topics such as condom use to protect themselves from both HIV and viral hepatitis.

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