Simultaneously High Prevalences of Hepatitis B and C Virus Infections in a Population in Putian County, China

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This study investigated a rare area of endemicity with a high prevalence of both hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, in Putian County, China. Among 1,050 subjects, the overall prevalence of HBsAg seropositivity was 15.8%, and that of anti-HCV seropositivity was 28.9%. Intrafamilial viral transmission might be the major cause of the high prevalence of HBV infection in this region. However, HCV infection was shown to be associated with the use of inadequately sterilized medical equipment.

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the major causes of chronic hepatitis, cirrhosis, and hepatocellular carcinoma (5). Few reports have addressed the simultaneously high prevalences of HBV and HCV infections among the general population in a single area. This study identified high prevalences of both HBV and HCV infections in a village of Putian County, Fujian province of China. All residents of the village over the age of 2 years were invited to participate. All subjects completed a questionnaire designed by the investigators to obtain the following information: participant's name, age, sex, and potential risk factors for viral transmission. This study was approved by the ethics committees of PLA General Hospital. Informed consent to participate was obtained from all adult individuals or parental/legal guardian of children participating.

Venous blood samples obtained from each subject were centrifuged (2,000 × g, 20 min, 4°C) to obtain serum. Anti-HCV antibodies and HBsAg were screened, respectively, using an HCV antibody test kit and HBsAg enzyme-linked immunosorbent assay (ELISA) kits (Asintec, Xiamen, China) according to the instructions provided by the manufacturer. Samples testing positive for HCV antibodies were confirmed using Abbott HCV enzyme immunoassay (EIA) reagent (Abbott, IL). HBsAg-positive samples were confirmed with Abbott HBsAg (V2) reagent. Samples testing positive in both serological tests were considered positive.

Continuous variables are expressed as the means ± standard deviations (SD) for those variables that were normally distributed.

Univariate analyses were performed to identify those variables that were significantly associated with HBV or HCV seropositivity. Subsequently, a backward stepwise multivariable logistic regression model was created by using all statistically significant variables that were identified in the univariate analyses. For each variable in the multivariable models, the odds ratio (OR) and 95% confidence interval (CI) were calculated. Statistical analysis was performed using SPSS software version 11.5 for Windows (SPSS, Inc., Chicago, IL), and a *P* value of <0.05 was considered statistically significant.

Detailed demographics and risk factor assessments for HBV and HCV infection were obtained from 1,050 subjects (Table 1). There were no professional blood donors, intravenous drug abusers, or persons with tattoos, and all subjects reported having one or fewer lifetime sexual partners. There was a low frequency of blood transfusions, surgical procedures, dental treatments (dental

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TABLE 1 Demographic and clinical characteristics of the 1,050 subjects enrolled in this study^a

Characteristic	No. (%) with indicated result			
	HBV HBsAg ^{±b} (<i>n</i> = 166)	HCV antibody ^{±b} (<i>n</i> = 303)	HBV/HCV coinfection (<i>n</i> = 51)	No HBV/HCV infection (<i>n</i> = 632)
Mean age (yr)	35.6 ± 15.5	47.7 ± 14.6	47.7 ± 13.0	26.0 ± 184.3
Male	71 (42.8)	113 (37.3)	24 (47.1)	303 (47.9)
Ever had a blood transfusion	0 (0)	2 (0.7)	0 (0)	3 (0.5)
Ever had surgery	3 (1.8)	21 (6.9)	3 (5.9)	5 (0.8)
Ever had dental treatment	12 (7.2)	42 (13.9)	9 (17.6)	16 (2.5)
Ever had gastrointestinal endoscopic examination	4 (2.4)	28 (9.2)	4 (7.8)	12 (1.9)
Household contact with HBV HBsAg ⁺ person	10 (6.0)	6 (2.0)	5 (9.8)	16 (2.5)
Household contact with anti-HCV ⁺ person	37 (22.3)	66 (21.8)	13 (25.5)	133 (21.0)

^a Characteristics are shown as the percent incidence and the absolute number of the groups by serologic test results. Ages are given as means ± SD. Superscript plus sign indicates seropositivity.

^b Includes HBV/HCV coinfection.

TABLE 2 Risk factors for HBsAg and anti-HCV seropositivity in the 1,050 subjects as calculated by multivariable logistic regression analysis^a

Characteristic	No.	HBV HBsAg ⁺				HCV antibody ⁺			
		No. (%) (n = 166)	Adjusted OR	95% CI	P value	No. (%) (n = 303)	Adjusted OR	95% CI	P value
Age (yr)			1.100	1.011–1.197	0.027		1.903	1.732–2.090	<0.001
<10	110	1 (0.9)				1 (0.9)			
10–19	249	35 (14.1)				7 (2.8)			
20–29	92	15 (16.3)				11 (12.0)			
30–39	233	52 (22.3)				81 (34.8)			
40–49	148	30 (20.3)				78 (52.7)			
50–59	107	22 (20.6)				58 (54.2)			
60–69	63	6 (9.5)				34 (54.0)			
≥70	48	5 (10.4)				33 (68.8)			
Gender			0.938	0.671–1.311	0.708		0.727	0.527–1.003	0.052
Male	463	71 (15.3)				113 (24.4)			
Female	587	95 (16.2)				190 (32.4)			
Ever had a blood transfusion			0.000	0.000	0.999		1.648	0.274–9.911	0.585
No	1,045	166 (15.9)				301 (28.8)			
At least one	5	0 (0)				2 (40.0)			
Ever had surgery			0.689	0.204–2.321	0.548		4.833	1.593–14.664	0.005
No	1,024	163 (15.9)				282 (27.5)			
At least one	26	3 (11.5)				21 (80.8)			
Ever had dental treatment			1.328	0.690–2.554	0.396		1.369	0.689–2.720	0.370
No	989	154 (15.6)				261 (26.4)			
At least one	61	12 (19.8)				42 (68.9)			
Ever had gastrointestinal endoscopic examination			0.583	0.204–1.656	0.310		3.413	1.512–7.705	0.003
No	1,010	162 (16.0)				275 (27.2)			
At least one	40	4 (10.0)				28 (70.0)			
Household contact with HBV HBsAg ⁺ person			3.226	1.445–7.203	0.004		0.698	0.279–1.748	0.443
Yes	27	10 (37.0)				6 (22.2)			
No	1,023	156 (15.2)				297 (29.0)			
Household contact with anti-HCV ⁺ person			1.076	0.722–1.605	0.718		1.047	0.756–1.448	0.784
Yes	223	37 (16.6)				66 (30.0)			
No	827	129 (15.6)				237 (28.6)			

^a Logistic regression models adjusted for age, gender, blood transfusion, surgery, dental treatment, gastrointestinal endoscopy, household contact with an HBV HBsAg-positive person, and household contact with an anti-HCV antibody-positive person. Superscript plus sign indicates seropositivity.

fillings, extractions of teeth, scaling of teeth, or endodontic root canal treatments), gastrointestinal endoscopic examinations, and household contacts with HBV-positive or HCV-positive people. The prevalence of HBsAg seropositivity was 15.8% (166/1,050), and anti-HCV seropositivity was 28.9% (303/1,050) among these subjects, about 2-fold and 9-fold greater, respectively, than that reported among the general population in China (7.2% and 3.2%, respectively) (2, 4). The prevalence of HBV/HCV coinfection was 4.9% (51/1,050).

The prevalence of HBsAg seropositivity was lowest in the population aged between 2 and 10 years (0.9%, 1/110) and increased rapidly in subjects after the age of 10 years (17.6%, 165/940), with the highest prevalence identified for those aged 30 to 59 years ($P = 0.027$) (Table 2).

The prevalence of anti-HCV seropositivity increased significantly with age ($P < 0.001$), with more than half of the subjects aged 40 to 69 years being infected with HCV and 68.8% (33/48) of those who were older than this being infected; the lowest preva-

lence was in subjects aged between 2 and 9 years (0.9%, 1/110) (Table 2).

In the univariate analyses, HBsAg seropositivity was significantly associated with age and household contact with HBV-positive people ($P < 0.05$). In the multivariable analysis, age (OR, 1.100; 95% CI, 1.011 to 1.197; $P = 0.027$) and household contact with HBV-positive people (OR, 3.226; 95% CI, 1.445 to 7.203; $P = 0.004$) were the variables that remained independently associated with HBV infection (Table 2).

In the univariate analyses, age, gender, surgical procedures, dental treatment, and gastrointestinal endoscopic examination were significantly associated with anti-HCV seropositivity ($P < 0.05$). However, age (OR, 1.903; 95% CI, 1.732 to 2.090; $P < 0.001$), surgical procedures (OR, 4.833; 95% CI, 1.593 to 14.644; $P = 0.005$), and gastrointestinal endoscopic examination (OR, 3.413; 95% CI, 1.512 to 7.705; $P = 0.003$) were the variables that remained independently associated with HCV infection in the multivariable analysis (Table 2).

The high prevalence of both HBV and HCV infections is unusual for this population, which has experienced rapid economic development and lacks the risk factors of injection drug use, professional blood donation, or sexual promiscuity. Investigation of HBV and HCV transmission routes is required to provide important public health information for all the populations in these villages in Putian County.

The prevalence of HBsAg seropositivity was significantly associated with age in this population, appearing as a single peak. However, a serosurvey conducted in 1992 indicated that the prevalence of HBsAg presented two peaks, one during childhood and the other in the 30- to 39-year-old age group (2, 7). Since 1992, routine neonate immunization with the hepatitis B vaccine has been recommended by the Ministry of Health of China. This vaccine has been combined with hepatitis B immunoglobulin at birth for infants born to HBsAg-positive mothers to interrupt perinatal transmission (1, 3). The peak during childhood has been eradicated throughout China, including in this population, as a result of the policy.

Data on HCV suggested possible iatrogenic transmission of HCV in this population, with the probability of exposure to inadequately sterilized medical equipment increasing with age. Sequence analysis of HCV HVR1 and NS5B discounted intrafamilial HCV transmission as the main cause of the high prevalence of HCV infection (6). The finding that surgical procedures and gastrointestinal endoscopic examination were independently associated with HCV infection suggests iatrogenic transmission involving inadequately sterilized medical equipment within this village. The common use of nondisposable syringe devices by medical personnel in China (noncertified/licensed medical practitioners, such as local dressers and nurses) until the 1990s is likely to have played an important role in the high prevalence of HCV infection in this population.

In conclusion, we reported a rare area of endemicity with a

high prevalence of both HBV and HCV infections. Intrafamilial viral transmission, via household contacts and mother-infant vertical transmission, might be the predominant cause of the high prevalence of HBV infection in this population. Further integrated measures designed to improve the efficacy of immunization and interrupt HBV transmission routes are required. Iatrogenic viral transmission was implicated as the main cause of the high prevalence of HCV infection, which is predicted to diminish with the use of disposable medical apparatuses. This study suggests that improved education regarding health issues and medical investment in rural areas of China and similar developing countries are required to tackle the high prevalence of HBV and HCV infection.

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REFERENCES

1. Chen DS. 2009. Hepatitis B vaccination: the key towards elimination and eradication of hepatitis B. *J. Hepatol.* **50**:805–816.
2. Liang X, et al. 2009. Epidemiological serosurvey of hepatitis B in China—declining HBV prevalence due to hepatitis B vaccination. *Vaccine* **27**:6550–6557.
3. Liang X, et al. 2009. Evaluation of the impact of hepatitis B vaccination among children born during 1992–2005 in China. *J. Infect. Dis.* **200**:39–47.
4. Liu F, et al. 2009. Hepatitis C seroprevalence and associated risk factors, Anyang, China. *Emerg. Infect. Dis.* **15**:1819–1822.
5. Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. 2006. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *J. Hepatol.* **45**:529–538.
6. Shi S, Lu F, Yan L, Zhuang H. 2011. Intrafamilial viral transmission is not the main cause of the high prevalence of hepatic C virus infection in a village, Putian county, China. *J. Clin. Virol.* **51**:110–114.
7. Xia GL, et al. 1996. Prevalence of hepatitis B and C virus infections in the general Chinese population. Results from a nationwide cross-sectional seroepidemiologic study of hepatitis A, B, C, D, and E virus infections in China, 1992. *Int. Hepatol. Commun.* **5**:62–73.