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Contents

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Prospective Study

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Chang Moo Kang, MD, PhD, Associate Professor, Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Yonsei University, Pancreaticobiliary Cancer Clinic, Yonsei Cancer Center, Severance Hospital, Seoul 120-752, South Korea

AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

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Ze-Mao Gong, Director
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Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
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Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
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PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
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ORIGINAL ARTICLE

Retrospective Study

Epidemiological features of chronic hepatitis C infection caused by remunerated blood donors: A nearly 27-year period survey

You-Wen Tan, Yan Tao, Long-Gen Liu, Yun Ye, Xin-Bei Zhou, Li Chen, Cong He

You-Wen Tan, Yan Tao, Yun Ye, Xin-Bei Zhou, Li Chen, Cong He, Department of Hepatology, The Third Hospital of Zhenjiang Affiliated Jiangsu University, Zhenjiang 212003, Jiangsu Province, China

Long-Gen Liu, Department of Hepatology, The Third People's Hospital of Changzhou, Changzhou 213001, Jiangsu Province, China

ORCID number: You-Wen Tan (0000-0002-5464-1407); Yan Tao (0000-0002-3502-6548); Long-Gen Liu (0000-0001-8652-2499); Yun Ye (0000-0002-0286-7359); Xin-Bei Zhou (0000-0002-8220-0377); Li Chen (0000-0002-9045-6292); Cong He (0000-0003-4085-5380).

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Correspondence to: You-Wen Tan, PhD, Attending Doctor, Chief Doctor, Department of Hepatology, The Third Hospital of Zhenjiang Affiliated Jiangsu University No. 300, Daijiamen, Runzhou Distinct, Zhenjiang 212003, Jiangsu Province, China. tyw915@sina.com
Telephone: +86-13914567088
Fax: +86-511-88970796

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Abstract

AIM

To understand the prevalence of hepatitis C virus (HCV) infection in blood donors over a nearly 27-year interval and to explore the factors that affect the outcome of HCV infection.

METHODS

A retrospective and cross-sectional study was conducted. The participants, mostly plasma donors, were selected from three administrative villages in the Jiangsu province in Eastern China. A questionnaire was administered among the villagers who had a history of blood donation from the late 1980s to the early 1990s. All participants underwent physical examination, liver B-ultrasonography, and liver stiffness measurement. In addition, 10 mL of blood was collected from each participant to measure simple liver function parameters (albumin, alanine aminotransferase, aspirate aminotransferase), blood factors (platelet), and for hepatitis B surface antigen, antiHCV, and antihuman immunodeficiency virus detection. HCV RNA detection, HCV genotyping, and other tests were carried out in antiHCV-positive patients.

RESULTS

After a median of 27 years (25-31 years) from the last blood donation to the time of survey, a total of 1694 participants were investigated, and the antiHCV-positive individuals were categorized into three groups: blood donors (*n* = 12, 3.3%), plasma donors (*n* = 534, 68.5%), and mixed donors (*n* = 324, 58.8%). A total of 592 (68.05%) patients had detectable HCV RNA, and 91.9% had genotype 1b. A total of 161 (27.2%, 161/592) patients with chronic HCV were considered to have cirrhosis with a liver stiffness measurement level higher than 12 kPa. Multiple logistic (binary) regression analysis results showed that platelet and IgG levels were associated with cirrhosis.

CONCLUSION

The nearly 27-year interval investigation revealed that chronic hepatitis C infection is a very serious public health problem in Eastern China. Plasma donation and subsequent return of blood cells to the donor are the main causes of hepatitis C infection. The main HCV genotype is 1b. Nearly 28% of cases progressed to cirrhosis. Age, especially over 60 years, and regular drinking habits were risk factors associated with cirrhosis.

Key words: Blood donor; Hepatitis C; Cross-sectional study; Epidemiologic; China

Core tip: A retrospective and cross-sectional study was conducted. A total of 1694 participants were investigated and categorized into three groups: 2 (3.3%), 534 (68.5%), and 324 (58.8%) patients positive for anti-hepatitis C virus (HCV) in blood donor, single plasma donor, and mixed donor groups, respectively. A total of 592 (68.05%) cases had detectable HCV RNA, and genotype 1b accounted for 91.9%. A total of 161 (27.2%, 161/592) patients with chronic HCV were considered to have cirrhosis with a liver stiffness measurement level of more than 12 kPa. Multiple logistic (binary) regression analysis results showed that platelet and IgG levels were associated with cirrhosis.

Tan YW, Tao Y, Liu LG, Ye Y, Zhou XB, Chen L, He C. Epidemiological features of chronic hepatitis C infection caused by remunerated blood donors: A nearly 27-year period survey. *World J Gastroenterol* 2018; 24(11): 1250-1258 Available from: URL: http://www.wjgnet.com/1007-9327/full/v24/i11/1250.htm DOI: http://dx.doi.org/10.3748/wjg.v24.i11.1250

INTRODUCTION

Hepatitis C infection is a major global public health problem. The World Health Organization estimated that the global hepatitis C virus (HCV) infection rate is about 2.8% and that about 170 million people are infected with chronic HCV. Approximately 350000 people die each year from hepatitis C-related liver diseases[1,2]. However, because of the occult nature of HCV, most people who are infected have no knowledge of their HCV infection; thus, the global incidence of chronic hepatitis C (CHC) is not clear. A Serum Hepatitis C Epidemiology Survey carried out in 2006 in China showed that the general population aged 1-59 years has an antiHCV-carrying rate of 0.43% and in the global range, HCV infection has low prevalence in some areas[3].

HCV is mainly transmitted through contact with the blood of an infected person; thereby, blood donors, especially plasma donors, are high-risk groups for HCV infection[4]. A study in remunerated blood donors reported an increased HCV infection rate of 15.53%[5] due to the use of nonsterile medical devices and other reasons.

The phenomenon of remunerated blood donation has been reported to occur in underdeveloped rural areas with low economic status, from the late 1980s to the early 1990s. Moreover, most of these hepatitis C-infected individuals had no history of seeking any medical assistance and had no knowledge about their HCV status; although, a considerable proportion of infections among those who have progressed to cirrhosis or even to hepatocellular carcinoma (HCC) were found.

The natural history of HCV has not been as fully delineated as that of hepatitis B virus[6]. Some epidemiological studies suggest that an estimated nearly 55%-85% of the individuals infected with acute hepatitis C will develop CHC, and nearly 5%-15% of patients with CHC will progress to cirrhosis after 20 years[7]. However, the conclusions of these epidemiological studies differ widely and lack longer epidemiological surveys. The main reason is the lack of a relatively fixed CHC epidemiological population.

A CHC population infected through plasma apheresis donation has a relatively consistent infection time and place. Most of these patients with hepatitis C infection did not seek medical assistance. These characteristics have created a unique advantage for the study of the natural history of hepatitis C.

We, therefore, chose to study the natural administrative villages in Jiangsu, a province in Eastern China where most villagers are plasma donors, in order to further understand the prevalence and the prognosis of HCV infection over nearly 30 years and to explore the factors that affect the outcome of this infection.

MATERIALS AND METHODS

Ethics statement

The study was approved by the Medical Ethics Committee of the Third Hospital of Zhenjiang Affiliated Jiangsu University, and written informed consent was obtained from each patient prior to participation. The study was conducted in compliance with the Declaration of Helsinki.

Participation and methods

A retrospective and cross-sectional study was conducted. The research team was composed of a staff of more than 20 trained individuals, including specialist doctors, technicians, community doctors, nurses, epidemiological researchers, medical graduate students, *etc*. Before the survey, a formal survey plan was drafted in advance and a standard questionnaire formulated. Two weeks prior to the survey, a research representative informed participants about the questionnaire and their physical and ultrasound examinations, and provided information about any matter requiring attention. Signed informed consent was obtained before the study started in the community hospital at the appointed time.

Research participation: The participants were selected from three administrative villages in the Jiangsu province in Eastern China, where most people are plasma donors, and the questionnaires were carried out among the villagers who had a history of plasma extraction. The participants had signed written informed consent. The inclusion criteria were the following: (1) a history of remunerated blood donation from the late 1980s to the early 1990s; (2) age above 40 years; (3) voluntary provision of contact information; and (4) no HCV treatment performed. Qualified subjects participated in the health examination and questionnaire from March to May 2017.

Investigation methods: The researchers conducted a unified training. The questionnaire submitted to the patients included: social demographic characteristics; history of common diseases, viral hepatitis, family diseases, and remunerated blood donations; and blood transfusion methods. All participants underwent physical examination, liver B-ultrasound and liver stiffness measurement (LSM). In addition, 10 mL of blood were collected for simple liver function parameter analysis [albumin (ALB), alanine aminotransferase (ALT); aspartate aminotransferase (AST)], blood routine [platelet (PLT)], and hepatitis B surface antigen (HBsAg), antiHCV, and antihuman immunodeficiency virus (HIV) detection.

Detection for HCV RNA, HCV genotyping, and other tests were carried out in antiHCV-positive patients. HCV RNA from subjects' sera was quantified in fresh or well-preserved stored samples by commercial quantitative assays, such as real-time PCR (COBAS AmpliPrep/COBAS *Taq*Man HCV Test; Roche, DaAn Gene Co., Nanjing, China). The HCV genotype was assessed in all patients with detectable HCV RNA. We used a PCR assay based on reverse transcription of the HCV core region with genotype-specific primers, in accordance with the international classification (*i.e.* Ⅰa, Ⅰb, Ⅱa, Ⅱb, Ⅲ, Ⅳ, Ⅴ and Ⅵ) (DaAn Gene Co,). Antinuclear antibody (ANA) and smooth muscle actin (SMA) determination was carried out using indirect immunofluorescence.

LSM

LSM using transient elastography (TE) (FibroScan502®; Echosens, Paris, France) was performed with the 3.5 MHz standard probe operated by a skillful operator (experience: > 10000 measurements) in a blinded manner. As previously described, the examination was carried out with the patient lying down in a supine position with the right arm placed behind the head. The tip of the probe transducer was placed on the skin between the ribs at the level of the right lobe of the liver, exerting an adequate pressure on it. The results were expressed in kPa, and each LSM value corresponds to the median of 10 validated measurements[8]. An examination was considered successful and reliable if the interquartile range (IQR)/median for LSM was ⩽ 30% or the LSM was < 7.1 kPa when the IQR/median for LSM was > 30%[9]. For the diagnosis of liver cirrhosis, a cut-off value of 12 kPa was used.

Statistical analysis

Continuous variables are given as median (range) or mean ± SD and categorical variables as frequencies or percentages (%) of patients. All data of demographic and clinical features were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 21.0 (IBM Corp., Armonk, NY, United States). Chi-squared and Fisher's exact tests were performed for categorical variables, while Student's *t*-test or one-way analysis of variance was used for group comparisons of parametric quantitative data. Multinomial (binary) logistic regression was performed to evaluate factors predicting CHC and cirrhosis. All *P* values were two-

Table 1 Demographic and clinical characteristics of remunerated blood donors

	Blood donors, *n* = 363	Single plasma donors, *n* = 780	Blood and plasma donors, *n* = 551	*P* value
Age in yr	56.8 ± 13.2	57.2 ± 11.3	57.1 ± 9.4	0.882[1]
⩾ 40, < 50	56 (15.4)	83 (10.6)	68 (12.3)	0.07
⩾ 50, < 60	203 (55.9)	501 (64.2)	336 (61.0)	
⩾ 60	104 (28.7)	196 (25.1)	147 (26.7)	
Sex				
Male	123 (33.92)	315 (36.5)	211 (38.3)	0.109[2]
Female	240 (66.1)	465 (63.5)	340 (61.5)	
BMI	25.52 ± 4.32	25.36 ± 4.11	25.45 ± 3.22	0.353[1]
< 25	178 (49)	395 (50.6)	294 (53.4)	0.167[2]
⩾ 25, < 28	130 (35.8)	284 (36.4)	169 (30.7)	
⩾ 28	55 (15.2)	101 (12.9)	88 (16)	
PLT as × 10^9/L	207.3 ± 64.8	161.8 ± 55.4	176.3 ± 63.1	< 0.001[1]
ALB in g/L	42.3 ± 3.5	41.4 ± 4.7	43.3 ± 4.5	0.513[1]
ALT in U/L	27.4 ± 6.5	63.2 ± 18.7	52.6 ± 15.4	< 0.001[1]
AST in U/L	23.5 ± 7.4	55.4 ± 12.9	44.5 ± 22.6	< 0.001[1]
Anti-HCV				
Positive	12 (3.3)	534 (68.5)	324 (58.8)	< 0.001[2]
Negative	351 (96.7)	246 (31.5)	227 (41.29)	
HBsAg				
Positive	2 (0.6)	3 (0.4)	1 (0.2)	0.643[3]
Negative	361 (99.4)	777 (99.6)	550 (99.8)	
LSM in kPa	5.56 ± 2.64	7.37 ± 3.62	6.54 ± 3.54	< 0.001[1]
⩾ 9	2 (0.6)	224 (28.7)	122 (22.1)	< 0.001[2]
< 9, ⩾ 6	20 (5.5)	313 (40.1)	287 (52.1)	
< 6	341 (93.9)	243 (31.2)	142 (25.8)	
Blood donated frequency times				
⩾ 10	212 (58.4)	245 (31.4)	187 (33.9)	< 0.001[2]
< 10, ⩾ 5	120 (33.1)	352 (45.1)	202 (36.7)	
< 5	31 (8.5)	183 (23.5)	162 (29.4)	
Interval time from last donated blood to survey in yr	27.56 ± 2.11	27.65 ± 3.02	27.84 ± 2.54	0.453[1]
Refused donated by elevated ALT				
Yes	37 (10.2)	317 (40.6)	195 (35.4)	< 0.001[2]
No	326 (89.8)	463 (59.4)	356 (64.6)	

Data are presented as *n* (%). The normal range of ALT and AST are 5-40 U/L, PLT is 100-300 × 10^9/L, ALB is 35-55 g/L. [1]One-way analysis; [2]Pearson Chi-Squared; [3]Fisher's exact test. ALB: Albumin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BMI: Body mass index; LSM: Liver stiffness measurement; PLT: Platelet.

sided.

RESULTS

Demographic and clinical characteristics of remunerated blood donors

In this survey, we investigated a total of 1694 participants after a median of 27 years (25-31 years) from the last blood donation to the moment of survey, including 363 blood donors, 780 plasma donors and 551 mixed blood donors. We detected 870 antiHCV-positive cases, 6 HBsAg-positive cases and no cases of HIV infection. As shown in Table 1, we analyzed age, sex, body mass index (BMI; < 25; ⩾ 25, < 28; ⩾ 28), PLT, ALB, ALT, AST, antiHCV (positive, negative), HBsAg (positive, negative), LSM (< 6; ⩾ 6, < 9; ⩾ 9), frequency of blood donation (< 5 ; ⩾ 5 < 10; ⩾ 10), and rejection of blood donation owing to elevated ALT (yes, no). The differences in PLT, ALT, AST, LSM, frequency of blood donation, and rejection of blood donation owing to elevated ALT were statistically significant ($P < 0.05$) among different blood donation mode groups. In particular, we observed 12 (3.3%), 534 (68.5%) and 324 (58.8%) antiHCV-positive patients in the blood donor, plasma donor and mixed donor groups, respectively.

Demographic and clinical characteristics of CHC

A total of 870 participants were antiHCV-positive; among them, 592 (68.05%) had detectable HCV RNA, were diagnosed with CHC and categorized to the CHC group, whereas 278 (31.95%) had undetectable HCV RNA and were categorized to the no CHC group. Table 2 shows an analysis of age, sex, BMI, (< 25; ⩾ 25, < 28; ⩾ 28), PLT, ALB, ALT, AST, SMA (positive, negative), ANA (positive, negative), immunoglobulin (IgG; normal, elevated), LSM (< 6; ⩾ 6, < 9; ⩾ 9), frequency of blood donation (< 5; ⩾ 5 < 10; ⩾ 10), and rejection of blood donation due to elevated ALT (yes, no). Differences in age, BMI, homeostatic model assessment of insulin resistance (HOMA-IR), ALT, AST, PLT and LSM were statistically significant ($P < 0.05$)

Table 2 Demographic and clinical characteristics of hepatitis C virus in remunerated blood donors and multiple logistic regression analysis of factors associated with hepatitis C virus

	CHC, *n* = 592	No CHC, *n* = 278	*P* value	Multivariate[4]			
				OR	95%CI	Wald	*P* value
Age in yr	55.4 ± 13.2	58.5 ± 9.4	< 0.001[1]	1.642	0.426-11.164	3.012	0.013
⩾ 40, < 50	121 (20.4)	35 (12.6)	0.003[2]		1		
⩾ 50, < 60	356 (60.1)	168 (60.4)		3.542	0.521-13.254	1.534	0.435
⩾ 60	115 (19.4)	75 (27.0)		11.226	0.065-137.53	5.322	0.004
Sex							
Male	277 (46.8)	111 (39.9)	0.058[2]		1		
Female	315 (53.2)	167 (60.1)		0.233	0.054-6.634	1.004	0.364
Alcohol consumption				0.532	0.147-1.647	0.853	0.547
Never	441 (74.5)	175 (62.9)	0.002[2]	0.436	0.124-1.006	1.075	0.443
Occasional	95 (16.0)	68 (24.5)		0.876	0.857-1.354	1.446	0.374
Often	56 (9.5)	35 (12.6)		1.231	0.843-1.556	0.667	0.432
BMI	24.12 ± 2.32	25.45 ± 3.22	< 0.001[1]	0.889	0.674-1.327	0.896	0.547
< 25	278 (47.0)	194 (69.8)	< 0.001[2]	1.216	0.536-1.625	0.034	0.646
⩾ 25, < 28	230 (38.9)	69 (24.8)		7.233	0.054-66.63	1.534	0.343
⩾ 28	84 (14.2)	15 (5.4)		4.365	0.643-22.534	1.543	0.113
HOMA-IR	1.53 ± 0.48	1.31 ± 0.52	< 0.001[1]	1.002	0.864-1.007	0.984	0.657
PLT as × 10^9/L	164.3 ± 64.8	196.3 ± 73.1	< 0.001[1]	3.112	1.475-121.153	16.886	< 0.001
ALB in g/L	42.3 ± 3.5	43.3 ± 4.5	0.513[1]	0.576	0.645-1.2147	0.543	0.674
ALT in U/L	67.4 ± 26.5	22.6 ± 15.4	< 0.001[1]	3.216	1.036-121.625	25.034	< 0.001
AST in U/L	53.5 ± 17.4	24.5 ± 10.6	< 0.001[1]	2.578	0.937-76.354	26.332	< 0.001
SMA							
Negative	517 (87.3)	262 (94.2)	0.002[2]		1		
Positive	75 (12.7)	16 (5.8)		1.146	0.545-1.654	0.543	0.653
ANA							
Negative	477 (80.6)	244 (87.8)	0.009[2]		1		
Positive	115 (19.4)	34 (12.2)		1.423	0.587-1.001	0.123	0.886
IgG							
Normal	271 (45.8)	261 (93.9)	< 0.001[2]		1		
Elevated	321(54.2)	17 (6.1)		6.001	0.957-12.353	6.075	< 0.001
LSM in kPa	7.67 ± 4.43	4.12 ± 2.25	< 0.001[1]	0.233	0.054-6.634	1.004	0.364
< 6	155 (26.2)	241 (86.7)	< 0.001[2]		1		
< 9, ⩾ 6	211 (35.6)	31 (11.2)		0.532	0.147-1.647	0.853	0.547
⩾ 9	226 (38.2)	6 (2.2)		2.436	0.124-11.776	7.075	< 0.001
Blood donated frequency times	8.67 ± 6.43	8.42 ± 6.25	0.107[1]	1.233	0.874-1.134	1.032	0.832
< 5	139 (23.5)	62 (22.3)	0.101[2]		1		
< 10, ⩾ 5	252 (42.6)	102 (36.7)		0.932	0.927-1.433	1.032	0.883
⩾ 10	201 (34.0)	114 (41.0)		0.247	0.257-1.754	1.054	0.664
Refused donated by elevated ALT							
No	377 (63.7)	148 (53.2)	0.003[3]		1		
Yes	215 (36.3)	130 (46.8)		1.668	1.061-3.143	4.804	0.027

Data are presented as *n* (%). Alcohol consumption: Often, the ethanol intake per week was more than 140 g in men (70 g in women) in the past 12 mo; Occasional, the ethanol intake per week was less than 140 g in men (70 g in women) in the past 12 mo. [1]One-way analysis; [2]Pearson's chi-square; [3]Fisher's exact test; [4]Binary logistic regression. ALB: Albumin; ALT: Alanine aminotransferase; ANA: Antinuclear antibody; AST: Aspartate aminotransferase; BMI: Body mass index; CI: Confidence interval; LSM: Liver stiffness measurement; OR: Odds ratio; SMA: Smooth muscle actin; PLT: Platelet.

between the HCV and no HCV groups. However, ALB, frequency of blood donation and refusal of donation by elevated ALT were not significantly different.

Demographic and clinical characteristics of cirrhosis caused by HCV infection and multiple logistic regression analysis associated with cirrhosis

A total of 161 (27.2%, 161/592) patients with CHC were diagnosed with cirrhosis, having an LSM value higher than 12 kPa. Among them, 431 patients were diagnosed with CHC. Table 3 shows an analysis of the age, sex, alcohol consumption (never, occasional, often), BMI (< 25; ⩾ 25, < 28; ⩾ 28), PLT, ALB, ALT, AST, HCV RNA (LgIU/mL, ⩾ 3,< 5; ⩾ 5), genotype (Ⅰ, Ⅱ, Ⅲ), frequency of blood donation (< 5 ; ⩾ 5 < 10; ⩾ 10), and rejection of blood donation due to elevated ALT (yes, no). Differences in age, alcohol consumption, PLT and IgG were statistically significant ($P < 0.05$) between the cirrhosis and CHC groups. However, sex, BMI, ALB, ALT, AST, SMA, ANA, HCV RNA, genotype, frequency of blood donation and rejection of blood donation due to elevated ALT were not significantly different. When the LSM level higher than 12 kPa was considered a binary dependent variable, multiple logistic (binary) regression analysis was used to assess factors associated with cirrhosis and CHC (Table 3).

Table 3 Demographic and clinical characteristics of cirrhosis by hepatitis C virus infection in remunerated blood donors and multiple logistic regression analysis of factors associated with cirrhosis

	Cirrhosis by HCV, *n* = 161	CHC, *n* = 431	*P* value	Multivariate[4]			
				OR	95%CI	Wald	*P* value
Age in yr	58.4 ± 13.2	56.5 ± 9.4	< 0.001[1]	2.143	0.553-6.453	4.543	0.002
⩾ 40, < 50	41 (25.43)	80 (18.6)	0.034[2]		1		
⩾ 50, < 60	82 (50.9)	270 (62.6)		2.443	0.242-7.345	1.423	0.065
⩾ 60	38 (23.6)	81 (18.8)		3.223	0.124-14.344	3.153	0.021
Sex							
Male	75 (46.6)	202 (46.9)	0.951[2]		1		
Female	86 (53.4)	229 (53.1)		1.223	0.112-6.765	0.653	0.445
Alcohol consumption							
Never	97 (60.2)	344 (79.8)	< 0.001[2]		1		
Occasional	40 (24.8)	55 (12.8)		0.879	0.647-2.654	2.753	0.152
Often	24 (14.9)	32 (7.4)		1.004	0.875-1.744	3.057	0.005
BMI	24.12 ± 2.32	25.45 ± 3.22	0.353[1]	0.647	0.465-1.632	4.135	0.432
< 25	78 (48.4)	200 (46.4)	0.108[2]		1		
⩾ 25, < 28	68 (42.2)	162 (37.6)		1.242	0.574-1.735	0.536	0.438
⩾ 28	15 (9.3)	69 (16)		0.665	0.426-1.645	0.476	0.537
HOMA-IR	1.53 ± 0.48	1.51 ± 0.52	0.556	0.023	0.772-1.423	0.365	0.221
PLT as × 10^9/L	147.3 ± 55.7	176.3 ± 84.2	< 0.001[1]	1.314	0.022-1.463	3.647	0.013
ALB in g/L	42.3 ± 3.5	43.3 ± 4.5	0.513[1]	0.864	0.707-1.364	1.557	0.675
ALT in U/L	67.4 ± 26.5	62.6 ± 25.4	0.113[1]	1.643	0.463-1.755	0.634	0.247
AST in U/L	53.5 ± 27.4	54.5 ± 22.6	0.201[1]	1.425	0.428-1.254	0.546	0.664
SMA							
Negative	144 (89.4)	373 (86.5)	0.346[2]		1		
Positive	17 (10.6)	58 (13.5)		0.526	0.537-1.843	1.034	0.536
ANA							
Negative	130 (80.7)	347 (80.5)	0.945[1]		1		
Positive	31 (19.3)	84 (19.5)		2.123	0.132-5.563	0.843	0.246
IgG							
Normal	60 (37.3)	205 (47.6)	0.025[2]		1		
Elevated	101 (62.7)	226 (52.4)		1.352	0.663-12.267	3.537	0.012
HCV RNA in LgIU/mL	7.12 ± 2.43	6.73 ± 2.533	0.067[1]	0.657	0.536-1.523	0.863	0.536
⩾ 3, < 5	22 (13.7)	51 (11.8)	0.546[2]		1		
⩾ 5	139 (86.3)	380 (88.2)		1.325	0.972-1.445	0.143	0.782
Genotype							
Ⅰ	152 (94.4)	390 (90.5)	0.310[2]		1		
Ⅱ	8 (5.0)	37 (8.6)		0.753	1.003-1.664	0.623	0.242
Ⅲ	1 (0.6)	4 (0.9)		1.862	1.182-1.635	0.845	0.118
Blood donated frequency times	8.67 ± 5.43	8.42 ± 6.25	0.107[1]	1.536	0.874-2.154	0.923	0.101
< 5	36 (22.4)	103 (23.9)	0.698[2]		1		
< 10, ⩾ 5	66 (41.0)	186 (43.2)		0.354	0.274-1.203	0.991	0.783
⩾ 10	59 (36.6)	142 (32.9)		1.024	0.154-2.163	0.332	0.224
Refused donated by elevated ALT							
No	94 (58.4)	243 (56.4)	0.661[2]		1		
Yes	67 (41.6)	188 (43.6)		0.012	0.037-1.002	0.682	0.563

Data are presented as *n* (%). Alcohol consumption: Often, the ethanol intake per week was more than 140 g in men (70 g in women) in the past 12 mo; Occasional, the ethanol intake per week was less than 140 g in men (70 g in women) in the past 12 mo. [1]One-way analysis; [2]Pearson's chi-square; [3]Fisher's exact test; [4]Binary logistic regression. ALB: Albumin; ALT: Alanine aminotransferase; ANA: Antinuclear antibody; AST: Aspirate aminotransferase; BMI: Body mass index; LSM: Liver stiffness measurement; SMA: Smooth muscle actin.

Using the "enter" method, the results suggested that age, alcohol consumption and PLT levels were associated with cirrhosis.

DISCUSSION

Hepatitis C is a blood-borne disease mainly transmitted by percutaneous exposure to contaminated blood and by unprotected sexual intercourse[10,11]. In the last century, from the late 1980s to the early 1990s, a large number of paid blood donors emerged in underdeveloped rural areas with a low economic status in Eastern China. Many blood donors were infected with HCV because of the use of contaminated medical devices. A total of 1694 participants were investigated, and 870 cases were positive for anti-HCV. In particular, we found 12 (3.3%), 534 (68.5%) and 324 (58.8%) patients positive against antiHCV in the blood donor, plasma donor and mixed donor groups, respectively.

The results showed that the blood donation method is the main cause of transmission of hepatitis C, and plasma donation in particular is the main causes of

hepatitis C infection. The rate of HCV infection in blood donors is 3.3%, quite similar to the average antiHCV-positivity rate of 3.2% in the general Chinese population according to the national epidemiological survey of HCV conducted from 1992 to 1995[12,13]. Some studies reported the transmission of hepatitis C in blood donors in the last decade in China[14-18]. However, this survey revealed that the blood donation method, in particular plasma apheresis, is the main cause of transmission of hepatitis C.

We also found that the frequency of blood donation in the plasma donor group was lower compared to the blood donor group, due to the more frequent rejection of blood donation in the plasma group because of elevated ALT. In other words, more plasma donors are likely to have been infected with HCV. The response of serum markers (ALT, AST and PLT) to liver damage in the plasma and mixed donor groups is higher than in the whole blood donor group. The HBsAg-positivity rate decreased because of the beginning of hepatitis B screening for blood donation.

HCV RNA was first detected in peripheral blood 1-3 wk after exposure to HCV[19]. Hepatitis C viremia not yet cleared 6 mo after exposure will progress to chronic infection. The hepatitis C chronicity rate is approximately 55%-85%[20-22]. Our survey interval of nearly 30 years shows that there are still 68% cases of detectable HCV RNA. Some studies have suggested that chronic predictive factors of HCV infection include male sex, age > 25 years, lack of symptoms after infection, race (African American), HIV infection, and immunosuppression[21]. The genetic background of the host may affect chronicity. IL-28B gene, human leukocyte antigen class 1 molecule HLA B57, and class Ⅱ molecules HLA DRB1 and DQBI allele polymorphism can affect HCV clearance[23-25]. For example, CC genotype at the rs12979860 site of the IL-28B gene leads to virus clearance, whereas TT is associated with a very low virus clearance[26,27].

In our study, age was a factor in the spontaneous clearance of the virus, but no sex-related differences in terms of HCV clearance were found. The increased levels of indicators of liver damage such as PLT, ALT, AST and LSM are considered the result of a chronic hepatitis C. Interestingly, blood donation due to elevated ALT reflects the activity of hepatitis C and indicates whether its current activity is beneficial to its spontaneous clearance.

HCV infection progresses slowly, up to 20 years after infection. The incidence of cirrhosis in children and young women is 2%-4%[28], in middle aged people infected due to blood transfusion 18%-30%[29], in plasma donors 1.4%-10.0%[7,30], and in the general population 5%-15%[26]. The factors that can promote disease progression include infection with HCV at age over 40 years, male sex, alcohol use (50 g/d or more in men, 70 g in women), HCV with HIV infection which leads to immune dysfunction[31,32], obesity, insulin resistance, hepatitis B virus infection, nonalcoholic fatty liver, high iron load in the liver, accompaniment of schistosomiasis infection, hepatotoxic drugs, and environmental pollution caused by toxic substances. Genetic factors can also promote disease progression[33,34].

Baseline liver tissue inflammation, necrosis and fibrosis stage are the best predictors of progression to cirrhosis. The incidence rate of cirrhosis of patients with CHC after a nearly 30-year interval is 27.2%, which was higher than in related studies[7,30]. Studying the incidence rate involved a long observation period, age, especially higher than 60 years, and regular drinking were risk factors for cirrhosis. Significantly increased levels of PLT and immunoglobulin are seen in cirrhosis.

HCV Ib and 2a genotypes were the most common in China, with genotype 1b (56.8%) being the highest, followed by genotypes 2 (24.1%) and 3 (9.1%). Genotypes 4 and 5 were not found, whereas genotype 6 (6.3%)[3] was found to be low. However, our study found that genotype 1b accounted for 91.9%, which shows heterogeneity in the distribution of hepatitis C genotypes in China.

In conclusion, this research over 27 years revealed that CHC infection remains a serious public health problem in Eastern China. Plasma donation is the main causes of hepatitis C infection. The main HCV genotype is 1b. After nearly 30 years of CHC, nearly 28% of cases progressed to cirrhosis. Age, especially greater than 60 years, and regular drinking habits were risk factors associated with cirrhosis.

ARTICLE HIGHLIGHTS

Research background

The natural history of hepatitis C virus (HCV) is still unclear. One of the main reasons why natural history is not clear is that the time of establishment of the infection is unclear. In this report, the authors followed many patients with HCV who can estimate the time of infection.

Research motivation

In the last century, from the late 1980s to the early 1990s, a large number of paid blood donors emerged in underdeveloped rural areas with a low economic status in Eastern China. Many blood donors were infected with HCV because of the use of contaminated medical devices.

Research objectives

The study aimed to understand the prevalence of HCV infection in blood donors over a nearly 27-year interval and to explore the factors that affect the outcome of HCV infection.

Research methods

A retrospective and cross-sectional study was conducted. The participants, mostly plasma donors, were selected from three administrative villages in the Jiangsu province in Eastern China. A questionnaire was administered among the villagers who had a history of blood donation from the late 1980s to the early 1990s. All participants underwent physical examination, liver B-ultrasonography, and liver stiffness measurement (LSM). In addition, 10 mL of blood was collected from each participant to measure simple liver function parameters [albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST)], blood factors [platelet (PLT)], and for hepatitis B surface antigen (HBsAg), antiHCV, and antihuman immunodeficiency virus

detection. HCV RNA detection, HCV genotyping, and other tests were carried out in antiHCV-positive patients.

Research results

After a median of 27 years (25-31 years) from the last blood donation to the time of survey, a total of 1694 participants were investigated, and the antiHCV-positive individuals were categorized into three groups: blood donors (*n* = 12, 3.3%), plasma donors (*n* = 534, 68.5%), and mixed donors (*n* = 324, 58.8%). A total of 592 (68.05%) patients had detectable HCV RNA, and 91.9% had genotype 1b. A total of 161 (27.2%, 161/592) patients with chronic hepatitis C (CHC) were considered to have cirrhosis, with an LSM level higher than 12 kPa. Multiple logistic (binary) regression analysis results showed that PLT and IgG levels were associated with cirrhosis.

Research conclusions

The nearly 27-year interval investigation revealed that CHC infection is a very serious public health problem in Eastern China. Plasma donation and subsequent return of blood cells to the donor are the main causes of hepatitis C infection. The main HCV genotype is 1b. Nearly 28% of cases progressed to cirrhosis. Age, especially over 60 years, and regular drinking habits were risk factors associated with cirrhosis.

Research perspectives

This research over 27 years revealed that CHC infection remains a serious public health problem in Eastern China. The epidemiological data in the present investigation may play an important role in focusing on the significance of public health in chronic HCV infection.

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