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Epidemiological characteristics and risk factors of hepatitis C virus genotype 1 infection: a national epidemiological survey of Chinese Han population

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Abstract. – OBJECTIVE: Hepatitis C virus (HCV) infection is a high morbidity disease in China. The aim of this study was to explore the latest distribution of HCV genotypes in China, mainly focusing on epidemiological characteristics and risk factors of HCV genotype 1 in Chinese Han population.

PATIENTS AND METHODS: 793 HCV-positive patients were enrolled from 21 hospitals across China. The association of epidemiological data with HCV genotype 1 and the potential risk factors was analyzed using univariate and multivariate logistic regression analysis.

RESULTS: The HCV genotype 1b was detected in 66.9% of 793 patients. The way of infection, disease course, HCV RNA level, history of blood transfusion and smoking were found to be significantly different between patients infected with HCV genotype 1 and non-genotype 1. The result of univariate logistic regression analysis showed that HCV genotype 1 infection has a close relationship with age, gender, smoking history, the way of infection, allergy, disease course, and HCV RNA level. Moreover, the HCV RNA level, disease course, and blood transfusion history were the related risk factors for infection of HCV genotype 1 as demonstrated by multivariate logistic regression analysis.

CONCLUSIONS: The HCV genotype 1 was still the main genotype of HCV infection in China. We should intensify HCV screening for those people who aged over 50 years and had a history of blood transfusion in China. The treatment of genotype 1 should be paid more attention in antiviral of HCV.

Key words:
Hepatitis C virus genotype 1, Epidemiology, Risk factors, Public healthcare.

Introduction

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease[1]. The total global prevalence of HCV infection was estimated to be 1.6% (1.3-2.1%)[2]. Among them, approximately 25-50 million individuals with chronic HCV infection were in China, corresponding about 15-30% of the total HCV-infected population worldwide[3,4]. As a developing country with the largest population in the world, the large HCV-infected population has posed a huge challenge for Chinese public healthcare.

HCV has been reported to exhibit high genetic diversity that characterized by regional variations in genotype prevalence[5]. Genotype 1 is the largest constituent part of HCV with the strongest infectious in China[6]. Infection of HCV genotype 1 has been reported to associate with treatment failure. Updated data of the prevalence of HCV genotypes, essential clinical epidemiology and risk factors analysis between patients infected with HCV genotype 1 and non-genotype 1 may contribute to guide public health strategies and improve the prevention of HCV infection. Therefore, a large sets of data enrolled from 21 hospitals of 11 provinces were collected to update the prevalence of HCV genotypes in China, and related epidemiologic parameters and risk factors of HCV genotype 1 were analyzed.

Patients and Methods

Patients

This study was approved by the Ethical Committee of Shuguang Hospital and written informed consent was obtained from the participants or their guardians. The data of 793 patients infected with chronic HCV were collected from 21 University affiliated hospitals across China from May 2009 to Jun 2015. All patients fulfilled the criteria for HCV infection[7]. Patients with other viral hepatitis, liver cirrhosis, or liver cancer were excluded from the study.

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HCV patients with other primary organ diseases (heart, kidney, lung, endocrine, metabolism, blood, and severe gastrointestinal tract) and mental disorders were excluded. Participants who were pregnant or lactating were also excluded. The samples were collected and stored at –80°C according to a uniform protocol designed by the central laboratory. The epidemiological information and potential risk factors were obtained within 7 days after enrollment.

Hepatic function index

Hepatic function indexes were tested in our central laboratory (Adicon Clinical Laboratory, Hangzhou, China) using automatic biochemical analyzer (Cobas Mira, Roche, Switzerland), including alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), total bilirubin (TBIL), direct bilirubin (DBIL), albumin (ALB) and globulin (GLB). The ALT, AST, ALP, GGT were examined by velocity method. TBIL and DBIL were examined by turbidimetry. ALB was examined by the bromocresol green method. GLB was examined by colorimetric method 8.

HCV genotypes

HCV genotype was conducted in the central lab (Adicon Clinical Laboratory, Hangzhou, China). The RNA examination, RT-PCR, PCR and electrophoresis were all performed by stand protocol. The PCR product was purified by enzyme purification amplification (KHB, Shanghai, China), and sequenced by ABI 3100 sequenator (Applied Biosystems, Carlsbad, CA, USA). The RNA level of HCV was analyzed by RT-PCR method in this study by using HCV RNA quantitative detection kit (KHB, Shanghai, China).

Histopathological analysis

The liver tissues were obtained by aspiration biopsy (Bard Magnum Biopsy Instrument, Covington, GA, USA) with the guidance of B ultrasound. The tissue selected should be longer than 1 cm, containing more than 4 portal areas. Inflammatory activity grading (G0-G4) and fibrosis staging (S0-S4) were evaluated according to the criteria proposed by the International Study Group for HCV.

Statistical Analysis

The quantitive data were analyzed by *t*-test, and enumeration data were analyzed by χ^2. Univariate and multivariate logistic regression analysis were analyzed using SPSS 17.0 software (Version 17, SPSS Inc., Chicago, IL, USA). *p*-values of less than 0.05 were considered statistically significant.

Results

The distribution of HCV genotypes

In this study, we found genotype 1b was the most common HCV genotype, accounting for 66.9% of all 793 samples, followed by genotypes 2, 3 and 6. Compared with genotype 1b, genotype 1a was rare. Genotypes 4 and 5 were not found (Table I). Our data was consisted with previously published articles[3].

Epidemiological parameters and risk factors between type 1 Genotype and non-type 1 genotype HCV infection

Age distribution, sex, smoking history, the way of infection, allergy history, disease course, and serum HCV RNA level were found to have significant differences between type 1 Genotype and non-type 1 genotype HCV infection (Table II). The number of patients older than 50 years old, female, smoking and with blood transfusion were significantly larger in HCV genotype 1 infection group than non-genotype 1 infection group.

The pathological results compared between HCV type 1 genotype and non-type 1 genotype infection

No significant difference was found in hepatic function index between the two groups. Pathological analysis was performed in 43 patients with HCV genotype 1 and 37 patients with non-genotype 1 HCV infection. The inflammation and fibrosis gradings were not found to have significant differences (Table III).

Univariate logistic regression analysis

Univariate logistic regression analysis was performed using the genotype 1 as the dependent

Table I. The distribution of HCV genotypes in 793 HCV patients.

Genotypes	1a	1b	2a	3a	3b	6
Distribution n (%)	10 (1.3)	531 (66.9)	165 (20.8)	35 (4.4)	23 (2.9)	29 (3.7)

Table II. Epidemiological parameters compare between type 1 Genotype and non-type 1 genotype HCV infection.

Epidemiological parameters	Genotype 1	Non-genotype 1	F/χ^2	p
Age (years)	45.72±14.64	43.57±13.62	2.470	0.048
Age (<30/30-50/>50 years) (n)	94/202/244	50/124/79	14.209	0.001
Gender (male/female)	257/284	140/112	4.457	0.035
Smoking (n)	78	55	7.014	0.008
Drinking (n)	83	43	0.461	0.497
Transfusion/intimate contact /sex/ drug/unknown/others (n)	350/10/2/10/123/46	116/3/1/18/70/44	38.246	<0.001
Allergy (n)	76	22	4.107	0.043
Course (years)	8.44±7.63	5.34±6.24	-5.178	<0.001
Log10 HCV RNA	6.16±1.12	5.89±1.18	2.722	0.003
ALT (IU/L)	74.98±70.81	78.81±70.42	1.152	0.500
AST (IU/L)	55.85±41.12	54.71±37.89	<0.001	0.723
ALB (g/L)	42.99±5.00	42.99±4.37	1.478	0.998
GLB (g/L)	32.00±6.06	31.75±5.75	0.178	0.589
TBIL (umol/L)	16.91±7.57	16.55±8.46	2.697	0.546
GGT (IU/L)	53.79±60.52	50.39±56.49	0.542	0.466
BMI (kg/m2)	23.38±3.86	23.20±3.42	0.72	0.522

Table III. The pathological results compared between genotype 1 and non-genotype 1 genotype HCV infection.

Pathological item	Genotype 1	Non-genotype 1	χ^2	p
Inflammatory score (0/1/2/3/4) (n)	0/14/20/9/0	0/10/23/3/1	4.451	0.217
Fibrosis score (0/1/2/3/4) (n)	2/17/14/7/3	2/12/12/8/3	0.636	0.959

variable (Y=1, Y=0), epidemiological data and the risk factors as independent variables. Results showed that age, gender, smoking history, way of infection, allergy, disease course, and HCV RNA level were the influence factors of HCV genotype 1, as shown in Table IV.

Multivariate logistic regression analysis

Variables obtained from univariate logistic regression analysis were imported into the multivariate regression equation using forward LR method. The results showed that the HCV RNA level, disease course, and blood transfusion history were risk factors for HCV genotype 1 (Table V).

Table IV. Univariate logistic regression analysis.

Epidemiological parameters	B	S.E.	Wald	Sig.	Exp (B)	95% CI for EXP (B)	
						Lower	Upper
Age (group variable)	0.289	0.104	7.755	0.005	1.335	1.035	1.689
Gender	0.323	0.153	4.444	0.035	1.381	1.023	1.865
Smoking	-0.516	0.196	6.923	0.009	0.597	0.407	0.877
Drinking	-0.140	0.206	0.460	0.489	0.870	0.581	1.302
Transfusion history	0.803	0.158	25.661	<0.001	2.231	1.636	3.004
Allergy	0.513	0.225	4.040	0.044	1.671	1.013	2.757
Course (years)	0.060	0.012	26.110	<0.001	1.061	1.038	1.086
Log10 HCV RNA	0.353	0.112	9.965	0.002	1.424	1.143	1.773
ALT (IU/L)	-0.032	0.155	0.043	0.835	0.986	0.715	1.311
AST (IU/L)	0.000	0.002	0.072	0.789	0.999	0.996	1.003
ALB (g/L)	0.000	0.016	0.000	0.998	1.000	0.969	1.032
GLB (g/L)	0.007	0.013	0.292	0.589	0.993	0.968	1.019
TBIL (umol/L)	-0.006	0.010	0.365	0.545	0.994	0.975	1.014
GGT (IU/L)	-0.001	0.001	0.529	0.467	0.999	0.996	1.002
BMI (kg/m2)	0.017	0.020	0.712	0.399	1.017	0.978	1.058

Discussion

According to virus RNA nucleotide sequence, the HCV can be divided into six main types numbered from 1-6. Among the genetic subtypes, genotype 1 is by far the most common HCV genotype worldwide[8]. Because of racial difference, the clinical manifestations and severity of disease may vary in patients with different genotypes. In literature, the RNA level of HCV genotype 1 is higher than that of other genotypes[9]. In this study, genotype 1 is the major genotype of HCV virus among Chinese Han population, and the viral load in patients with type 1 was significantly higher than that of the non-genotype 1 (p=0.003). It can be found that the distribution of HCV genotypes in China matches the world trends.

The patients in genotype 1 and non-genotype 1 groups have significant differences in age, gender, smoking history, way of infection, allergy history, disease course, and HCV RNA level. Some researchers showed that HCV genotype distribution has a close relationship with liver function[10, 11]. This relationship was not found in our study. The result in this study indicates that despite of the different outcome, patients with different HCV genotypes may suffer from the similar pathway to liver damage.

In univariate logistic regression analysis, gender and age can affect HCV genotype 1 infection. This study showed that women have a greater chance of suffering from genotype 1 infection, which may be connected with more opportunities to blood transfusion[12]. The prevalence of HCV genotype 1 was higher than the non-1 types in patients over 50-years old, but patients of 30-50 years old showed the opposite trend while there was no significant difference in patients less than 30 years old. This phenomenon may be caused by the clinically large-scale screening of HCV in 1990s[13]. HCV was firstly discovered in 1989[14], and its late discovery brought about a blanking period of nearly half a century of HCV prevention and treatment. That led to the increased prevalence of HCV genotype 1 in blood transfusion patients over 50-years old in China. After HCV was screened, the spread chance of the HCV genotype 1 through blood transfusion was significantly decreased and made the infection rate of patients during 30-50-years old declined. Therefore, patients with a history of blood transfusion should be get more emphasis on screening HCV in clinical, especially those older than 50 years.

In multivariate logistic regression analysis, HCV RNA level, disease course and history of blood transfusion were major factors that are affecting genotype 1 infection. In addition, much attention should also be paid to other risk factors such as drug use, lifestyle, and iatrogenic-related factors.

In treatment, although studies have shown that IL-28 b gene polymorphism is a powerful predictor affecting the curative effect of interferon therapy[15], IL28B rs12979860 CC allele in Chinese Han population type provided relatively good priority to the treatment effect[16]. Another study[17] showed that the availability of early biological response was not only affected by virus genotype but also related with the immune status of patients. However, control of high viral load is still the key to the treatment of HCV. According to this finding, the patients with HCV genotype 1 infection have a higher viral load, so more attention should be paid on genotype 1 during anti-virus HCV. However, the limitations of the present study should be acknowledged. The more detailed clinical information is needed to be analyzed in further study.

Conclusions

In this study, we update the distribution of HCV genotypes in China. These data may contribute to guide public health strategies and, therefore, improve the prevention of HCV infection.

Conflict of interest

All co-authors have no competing interests.

Table V. Multiariable logistic regression analysis.

Epidemiological parameters	B	S.E.	Wald	Sig.	Exp (B)	95% CI for EXP (B)	
						Lower	Upper
Log_{10} HCV RNA	0.339	0.119	8.118	0.004	1.404	1.112	1.773
Course	0.044	0.013	11.019	0.001	1.045	1.018	1.072
Transfusion history	0.517	0.181	8.149	0.004	1.676	1.176	2.309

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