JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Distribution and genotyping of hepatitis C virus (HCV) infection in Gansu province, China

Qiajun Du[1 #], Xinghong Wu[1 #], Linmei Chen[1], Youli Zhao[1], Hongwei Gao[1], Yan Fen[2], Shangdi Zhang[1], Shan Gao[1]

[1] Laboratory Medical Center of Lanzhou University Second Hospital, Lanzhou 730030, Gansu Proviince, China
[2] The Second People's Hospital of Lanzhou City, Lanzhou 730080, Gansu Province, China

Qiajun Du and Xinghong Wu should be regarded as co-first authors.

Abstract

Introduction: The distribution of common subtypes of hepatitis C virus (HCV) in Gansu province were analyzed. This information provided a theoretical basis for the selection of appropriate antiviral treatment regimens.

Methodology: We collected data on HCV antibody screening tests from 421,802 outpatients and inpatients at the Second Clinical Hospital of Lanzhou University from January 2018 to June 2022. Ribonucleic acid (RNA) viral load, HCV genotypes, and HCV quantification were analyzed retrospectively. The results of HCV positive detection rate, copy number, and genotype distribution were statistically analysed using SPSS 26.0.

Results: A total of 421,802 HCV antibody screenings were performed resulting in 4,558 positive cases (1.081%). In addition, 2,345 cases (1.302%) were positive with quantitative HCV antibodies in 180,157 outpatients and inpatients. Quantitative HCV virus RNA was further measured in 2592 outpatients and inpatients. There were 825 positive cases for HCV, with a positivity rate of 31.83%. High-sensitivity quantification of HCV-RNA was performed in 6538 patients, among which 1336 were HCV-RNA positive infections (positivity rate of 20.43%). Among the 1484 genotype tests, 4 genotypes and 10 subtypes were detected, including 4a, 1b, 2a, 2b, 3a, 3b, 6a, 6n, 1b/2a, and 2a/6a, with the majority of results from 2a (51.89%) and 1b (42.72%).

Conclusions: The most prevalent genetic subtype in HCV-positive patients in Gansu was 2a, followed by 1b. In addition, 8 genotype subtypes appeared: 1a, 2b, 3a, 3b, 6a, 6n, 1b/2a and 2a/6a. Understanding the distribution of HCV genes in Gansu province is of significance for the optimization of virus treatment.

Key words: HCV; epidemiology; genotype; subtype; Gansu province.

J Infect Dev Ctries 2024; 18(3):458-463. doi:10.3855/jidc.18331

(Received 06 April 2023 – Accepted 25 August 2023)

Introduction

Hepatitis C virus (HCV) infection can lead to acute or chronic infections, with an increased incidence of hepatic cirrhosis and cancer in some patients over time [1]. It is a global epidemic and China is one of the countries with the highest incidence rates of HCV infection. Needle use, blood transfusions, and drug use are the most common ways to transmit HCV. Thus, certain population groups, such as drug users may have a higher prevalence of HCV infection [2].

HCV, a virus with a single positive-strand RNA, has six genotypes based on variability in the genome sequence. The 6 genotypes include a total of 67 different subtypes [3]. Previous evidence has shown that different genotypes can affect the infectivity and treatment efficacy after HCV infection. In order to achieve optimal results, clinicians often choose tailored treatment regimens based on the results of HCV genotypes. In addition, HCV genetic distribution varies geographically. Some genotypes are predisposed to a specific geographic location, and the distribution of genetic subtypes varies depending on the population [4,5]. However, there is no information on HCV prevalence and the genetic subtypes among residents of Lanzhou City, Gansu, China.

The distribution of HCV genotypes from 2018 to 2022 was determined based on the HCV antibody testing results of patients treated at the Second Clinical Hospital of Lanzhou University. This study provided reliable epidemiological information for the prevalence of HCV infection in Lanzhou City, Gansu province, which may help select antiviral treatment regimens for different HCV subtypes to optimize treatment effects.

Table 1. Qualitative and quantitative results of HCV antibodies in all patients from January 2018 to June 2022.

Year	Number of HCV antibody tests	Number of positive HCV antibodies	Positive rate (%)	Number of quantitative HCV antibody tests	HCV antibody quantification > 1 (n)	Positive rate (%)
2018	109050	1241	1.138	——	——	——
2019	111438	1251	1.123	26071	329	1.262
2020	76682	825	1.076	57527	810	1.408
2021	83666	830	0.992	62492	852	1.363
2022	40972	411	1.003	34066	354	1.039
Total	421802	4558	1.081	180156	2345	1.302

HCV: hepatitis C virus.

Methodology

Study population

The outpatients and inpatients were tested with the HCV screening test at the Second Clinical Hospital of Lanzhou University, Gansu province, from January 2018 to June 2022. We used the laboratory information system (LIS) of the laboratory department to collect qualitative and quantitative HCV antibody test results from the patients. The HCV RNA viral load and genotyping status were also counted. Basic demographic characteristics, including age and gender were recorded. This study was approved by the Medical Ethics Committee of the Second Hospital of Lanzhou University. Written informed consent was received from all participants.

Specimen collection

The patients diagnosed with HCV were selected from the Second Hospital of Lanzhou University during 2018-2022 after positive detection of HCV RNA antibody and were tested with DAAN HCV RNA nucleic acid quantitative detection kit (PCR-fluorescent probe method; State Food and Drug Administration standard No. 3400209; DAAN Gene, Guangzhou, PRC). Patients with serum viral copy number greater than 1×10^3 copies/mL were tested for the HCV RNA genotype (Tappe HCV genotyping detection reagent; PCR-fluorescent probe method; State Food and Drug registration 20163400890; TiB, Xiamen, PRC).

Statistical analysis

The difference in the distribution of HCV genotypes was tested by the Chi-square test, and $p < 0.05$ was considered statistically significant. The data were statistically analyzed using SPSS 26.0 software.

Results

Qualitative and quantitative testing for HCV antibodies

The total number of positive HCV antibody qualitative tests was 222,817 males and 198,985 females among 421,802 patients examined at the Second Clinical Hospital of Lanzhou University from January 2018 to 2022, with an average age of 43.5 ± 22.78 years (ranging from 0 to 101). There were 4558 cases (1.08%) of positive HCV antibody (Table 1). Among them, patients aged 40-60 years had the largest numbers of positive antibodies, followed by the age group of > 60 years. A total of 2262 cases (49.63%) were detected in males, while 2296 cases (50.37%) were detected in females (Table 2).

The association analysis between the results of qualitative HCV antibody test and age and gender showed that there were significant differences in HCV antibody serology tests based on gender ($\chi^2 = 18.910$, $p < 0.001$). Additionally, HCV characterization results were re-differenced by age group ($\chi^2 = 1518.904$, $p < 0.001$) (Table 2).

In addition, a total of 180,157 patients were tested for quantitative HCV antibodies, as shown in Table 1,

Table 2. Age and gender distribution, in terms of the number of patients and percentage, of HCV antibody-positive patients and HCV antibody quantitative results (>1).

Year	Age ≤ 20 years		Age 20–40 years		Age 40–60 years		Age > 60 years	
	Male	Female	Male	Female	Male	Female	Male	Female
HCV antibody-positive								
2018	8 (0.18)	3 (0.07)	90 (1.97)	65 (1.43)	305 (6.69)	307 (6.74)	202 (4.43)	261 (5.73)
2019	2 (0.04)	6 (0.13)	87 (1.91)	86 (1.89)	269 (5.90)	284 (6.23)	255 (5.59)	262 (5.75)
2020	5 (0.11)	9 (0.20)	56 (1.23)	51 (1.12)	198 (4.34)	175 (3.84)	173 (3.80)	158 (3.47)
2021	0 (0.00)	5 (0.11)	46 (1.01)	38 (0.83)	204 (4.48)	211 (4.63)	163 (3.58)	163 (3.58)
2022	4 (0.09)	2 (0.04)	26 (0.57)	17 (0.37)	95 (2.08)	114 (2.50)	74 (1.62)	79 (1.73)
Total	19 (0.42)	25 (0.55)	305 (6.69)	257 (5.64)	1071 (23.50)	1091 (23.94)	867 (19.02)	923 (20.25)
HCV antibody quantitative results (> 1)								
2019	1 (0.04)	3 (0.13)	24 (1.02)	14 (0.60)	73 (3.11)	96 (4.09)	47 (2.00)	71 (3.03)
2020	3 (0.13)	6 (0.26)	46 (1.96)	41 (1.75)	197 (8.40)	186 (7.93)	175 (7.46)	156 (6.65)
2021	6 (0.26)	3 (0.13)	51 (2.17)	47 (2.00)	210 (8.96)	185 (7.89)	172 (7.33)	178 (7.59)
2022	0 (0.00)	0 (0.00)	27 (1.15)	10 (0.43)	98 (4.18)	95 (4.05)	63 (2.69)	61 (2.60)
Total	10 (0.43)	12 (0.51)	148 (6.30)	112 (4.78)	578 (24.65)	562 (23.97)	457 (19.49)	466 (19.87)

HCV: hepatitis C virus.

Table 3. HCV RNA quantification and high-sensitivity HCV RNA quantification from January 2018 to June 2022. The numbers indicate the number of patients.

Year	HCV RNA quantification tests (n)	HCV RNA quantification > 500 (n)	Rate (%)	High-sensitivity HCV RNA quantification tests (n)	High-sensitivity HCV RNA quantification > 15 (n)	Rate (%)
2018	936	309	33.013	1192	245	20.554
2019	600	202	33.667	1610	313	19.441
2020	482	166	34.440	1431	299	20.894
2021	409	108	26.401	1587	319	20.101
2022	165	40	24.242	718	160	22.284
Total	2592	825	31.83	6538	1336	20.43

HCV: hepatitis C virus.

among which 2,345 patients (1.30%) were regarded as HCV-positive (> 1). The age and gender of the 2,345 HCV antibody-positive patients are presented in Table 2, with 1,193 (50.87%) male patients and 1,152 (49.13%) female patients. HCV infection with positive results were concentrated in patients in the 40-60 years old group (48.61%), and in the > 60 year old group (39.36%). There were no statistically significant differences between the results of quantitative HCV antibody tests between different genders ($\chi^2 = 1.134$, $p = 0.287$). Nevertheless, HCV antibody quantification results varied statistically significantly between different age groups ($\chi^2 = 472.029$, $p < 0.001$).

HCV-RNA detection status

A total of 2,592 outpatients and inpatients had their HCV RNA quantified from January 2018 to June 2022. Out of them, 1,767 patients had negative results and 825 had positive results (results over 5.0E + 2), with a positive rate of 31.83% (Table 3). An analysis of the gender and age distributions of HCV-RNA quantification positive infections was shown in Table 4. As a result, HCV-RNA-positive infections occurred mainly in the 40-60 years age group, followed by the > 60 years age group, with a smaller proportion in the other age groups. The results of HCV-RNA quantification differed by gender and were statistically significant. Similarly, there was variability in HCV-RNA quantification results across different age groups ($\chi^2 = 99.483$, $p < 0.001$).

The results of high-sensitivity HCV-RNA quantification tests in 6,538 patients are shown in Table 3. A total of 1,336 patients had HCV-RNA positive infections (> 1.5E), including 664 female (49.70%) and 672 male (50.30%) patients. The majority of high-sensitivity HCV-RNA positive patients were in the 40-60 years group (52.99%) and the least were in the ≤ 20 years group (1.12%). The relationship between quantitative detection of high-sensitivity HCV-RNA and gender and age was shown in Table 4. There were significant differences in the results of high-sensitivity HCV-RNA testing in different genders ($\chi^2 = 12.449$, $p < 0.001$). Furthermore, the high-sensitivity HCV-RNA assay revealed statistically significant differences between age groups ($\chi^2 = 52.024$, $p < 0.001$).

HCV genotyping

The results of 1484 HCV genotype tests showed that there were 4 genotypes and 10 genotypic subtypes, including 1a, 1b, 2a, 2b, 3a, 3b, 6a, 6n, 1b/2a, and 2a/6a. The main genotypes were 2a and 1b, with an incidence of 770 (51.89%) and 634 (42.72%) cases, respectively. In addition, two different genetically mixed subtypes were present. The genotype of the patients is shown in

Table 4. Age and gender distribution of HCV RNA quantification (> $5E^{+2}$ IU/mL) and high-sensitivity HCV RNA quantification (> 15 IU/mL). The numbers indicate the number of patients and percentage.

Year	Age ≤ 20 years		Age 20–40 years		Age 40–60 years		Age > 60 years	
	Male	Female	Male	Female	Male	Female	Male	Female
Hepatitis C virus RNA quantification > $5E^{+2}$ IU/mL								
2018	3 (0.36)	2 (0.24)	28 (3.39)	13 (1.58)	86 (10.42)	63 (7.64)	49 (5.94)	65 (7.88)
2019	1 (0.12)	1 (0.12)	17 (2.06)	20 (2.42)	43 (5.21)	45 (5.45)	43 (5.21)	33 (4.00)
2020	1 (0.12)	2 (0.24)	7 (0.85)	6 (0.73)	47 (5.70)	31 (3.76)	34 (4.12)	38 (4.61)
2021	0 (0.00)	0 (0.00)	4 (0.48)	7 (0.85)	32 (3.88)	28 (3.39)	17 (2.06)	20 (2.42)
2022	0 (0.00)	0 (0.00)	1 (0.12)	4 (0.48)	9 (1.09)	12 (1.45)	9 (1.09)	5 (0.61)
Total	5 (0.61)	4 (0.48)	57 (6.91)	50 (6.06)	217 (26.30)	179 (21.70)	152 (18.42)	161 (19.52)
High-sensitivity hepatitis C virus RNA quantification > 15 IU/mL								
2018	3 (0.22)	1 (0.07)	27 (2.02)	26 (1.95)	51 (3.82)	80 (5.99)	26 (1.95)	31 (2.32)
2019	1 (0.07)	1 (0.07)	28 (2.10)	22 (1.65)	79 (5.91)	94 (7.04)	34 (2.54)	54 (4.04)
2020	2 (0.15)	3 (0.22)	23 (1.72)	26 (1.95)	74 (5.54)	77 (5.76)	42 (3.14)	52 (3.89)
2021	0 (0.00)	2 (0.15)	35 (2.62)	16 (1.20)	104 (7.78)	62 (4.64)	46 (3.44)	54 (4.04)
2022	1 (0.07)	1 (0.07)	11 (0.82)	5 (0.37)	51 (3.82)	36 (2.69)	34 (2.54)	21 (1.57)
Total	7 (0.52)	8 (0.60)	124 (9.28)	95 (7.11)	359 (26.87)	349 (26.12)	182 (13.62)	212 (15.87)

HCV: hepatitis C virus.

Table 5. HCV genotype subtype distribution from January 2018 to June 2022. The numbers indicate the number of patients.

Year	Genotype 1		Genotype 2		Genotype 3		Genotype 6		Hybrid subtype
	1a	1b	2a	2b	3a	3b	6a	6n	
2018	0	93	108	0	5	6	0	0	2
2019	2	169	208	0	5	12	0	1	0
2020	2	147	195	1	7	7	2	0	0
2021	0	156	187	0	6	8	4	0	0
2022	0	69	72	0	6	4	0	0	0
Total (%)	4 (0.27)	634 (42.72)	770 (51.89)	1 (0.07)	29 (1.95)	37 (2.49)	6 (0.40)	1 (0.07)	2 (0.13)

HCV: hepatitis C virus.

Table 5. Both male and female patients had 2a and 1b as their predominant genotypes, and the number of infected males was comparable to that of infected females. The distribution of HCV genotypes by gender showed statistically significant differences ($\chi^2 = 61.169$, $p < 0.001$). The males had more 3a and 3b genotypes than females, and the rest of the genotypes were present in about the same number of men and women. HCV genotype distributions differed statistically significantly in different age groups ($\chi^2 = 46.981$, $p = 0.003$), with highest distribution in the 40-60 years old group (Table 6).

Discussion

Globally, hepatitis C is a serious health problem that needs to be addressed. According to the World Health Organization (WHO) reports, around 71 million people are estimated to be infected with HCV worldwide [6]. HCV is typically diagnosed through three clinical laboratory tests: antibody testing for HCV, testing for HCV-RNA viral load, and genotyping [7]. Screening for HCV antibodies may delay the diagnosis of infection since seropositivity may occur weeks to months after viral exposure. Further, some hemodialysis or immunocompromised patients may have false-negative screening results [8]. Some studies have found that false-positive HCV tests may also be observed in patients with autoimmune diseases. Thus, molecular testing and subsequent genotyping tests are particularly important.

HCV-RNA genotype and subtype information are important for guiding the selection of treatment and prevention of recurrence. There is an association between HCV-RNA viral load and liver damage. In addition, evidence has shown that some genetic subtypes of HCV can be characterized by high viral loads of HCV-RNA [9]. Among Chinese HCV-infected patients, HCV 2a displays a higher viral load than other genotypes. The viral load and genotype of HCV infection should be determined before antiviral therapy because the optimal treatment for an individual depends on their viral load and HCV genotype. In addition, viral load and HCV subtype are crucial factors in determining the efficacy of therapeutic agents. In China, patients with chronic HCV infection are currently treated with a combination of pegylated interferon alpha (PEG-IFNa) and ribavirin (RBV, Pr) [4]. According to a randomized trial, genotype 1 infections were less responsive to interferon treatment compared with genotypes 2 and 3 [10]. Interferon-α (IFN-α) plus zinc is more effective in targeting genotype 1 [11]. Therefore, it is important to choose different treatment regimens for the three common genotypes.

The emergence of potent direct-acting antivirals (DAAs) has revolutionized the treatment of hepatitis C virus. However, due to high costs, large numbers of undiagnosed patients, high reinfection rates in certain risk groups and host and viral genetic differences directly affecting the efficacy of the same drug, the most appropriate antiviral therapy can be administered after the correct determination of HCV genotype [12]. In this study, the genotypes of 1484 HCV infected patients were predominantly 2a and 1b, which was consistent with the genotyping trend in the northwest of mainland China [9]. According to previous reports,

Table 6. Distribution of HCV genotypes in patients of different genders and age groups. The numbers indicate the number of patients and percentage.

Group	Genotype 1 (%)		Genotype 2 (%)		Genotype 3 (%)		Genotype 6 (%)		Hybrid subtype (%)	χ^2	*p*
	1a	1b	2a	2b	3a	3b	6a	6n			
Gender											
Male	1 (0.13)	328 (43.85)	358 (47.85)	1 (0.13)	26 (3.48)	28 (3.74)	4 (0.53)	1 (0.13)	1 (0.13)	61.169	0.000
Female	3 (0.41)	306 (41.58)	412 (55.98)	0 (0.00)	3 (0.41)	9 (1.22)	2 (0.27)	0 (0.00)	1 (0.14)		
Age (years)											
≤ 20	0 (0.00)	7 (46.67)	8 (53.33)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	46.981	0.003
20~40	0 (0.00)	121 (50.84)	101 (42.44)	0 (0.00)	7 (2.94)	5 (2.10)	3 (1.26)	0 (0.00)	1 (0.42)		
40~60	3 (0.36)	340 (41.16)	426 (51.57)	0 (0.00)	21 (2.54)	31 (3.75)	3 (0.36)	1 (0.12)	1 (0.12)		
> 60	1 (0.25)	166 (40.99)	235 (58.02)	1 (0.25)	1 (0.25)	1 (0.25)	0 (0.00)	0 (0.00)	0 (0.00)		

HCV: hepatitis C virus.

genotype 1b was the main prevalent subtype of HCV infection worldwide [5]. In Guizhou, China, the 6a strain is the most dominant in hepatitis C, which may be related to the fact that the samples are all HIV/HCV co-infected [13]. Latin American epidemiological statistics on hepatitis C show that genotype 1 is still the predominant hepatitis C type in Latin America; this is similar to the results of this study [14]. The same results have been confirmed in related studies in Japan [15]. Although mixed genotypes for HCV infection were rare in our country, this study found one case each with mixed genotypes in males and females. Additionally, different genotype distributions may reflect different modes of infection transmission. The widespread use of blood transfusions and blood products was found to be associated with the prevalence of HCV subtype 1b. Conversely, 1a was strongly linked to the use of intravenous drugs [16]. Accurate determination of HCV typing is essential to eliminate the threat of HCV to the public in Gansu province and to select a complete anti-HCV therapy [17].

Various studies have examined the relationship between the genotype of HCV infection and gender and age in China and abroad. There was variation in the genotyping of HCV based on gender and age groups in this study. Males and females may have different immune responses, with different HCV genotypes. This observation was similar to the study conducted by Uccellini and his group in the Americas [18]. In this study, a similar proportion of males and females with HCV infection underwent genotyping (50.40% versus 49.60%). Infection with genotype 2 is more common in women than in men, while genotypes 1 and 3 are more common in males. In addition, the proportion of genotype 3 in males was about three times higher than that in females. HCV genotyping was concentrated in the 40-60 years and > 60 years age groups, accounting for 82.95% of all cases. Furthermore, age-related differences may be related to transmission routes [19]. Contrary to the patients in 40-60 years old group, who had a wide range of infection modes, the patients in over-60 years age group might be infected with HCV primarily through transfusion. This study updated the genotype distribution characteristics in Gansu, China, and provided relevant information for individualized treatment as well as prevention of HCV infection.

This study had several limitations. First, due to consideration of the window of time of HCV infection, repeat testing to confirm the diagnosis was not excluded in this study. Patients on antiviral therapy at different points may have a different HCV-RNA viral load. As a result, we included patients with duplicate items in our statistical analysis. In addition, the detailed information of baseline clinical characteristics, including disease history and concomitant therapies was not available for the patients included in the study.

Conclusions

In this study, we determined the detection rates of different HCV testing methods, and explored the distribution of HCV infection in Gansu province, China. Furthermore, the genotypes in the Gansu region showed a polygenic distribution, and varied in different gender and age groups. The results of the study may help guide the treatment and prevention of HCV infection.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Medical Ethics Committee of the Second Hospital of Lanzhou University [2018-A046]. Written informed consent was received from all participants.

Consent for publication

Informed consent to publish was obtained from the study participants.

Data availability statement

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Funding

This study was supported by National Natural Science Foundation of China (NO.32060231); GANSU Natural Science Foundation (NO. 21JR1RA138; NO. 21JR1RA130; NO. 22JR5RA962; NO. 22JR11RA055); Cuying Science and Technology innovation plan project (CY2019-BJ05); and Gansu Educational Technology Innovation Project (2020B-047).

Authors' contributions

QD: literature research and manuscript review; QD, SG: manuscript preparation; XW: clinical and experimental studies; LC, YF: data acquisition; YZ: statistical analysis; HG: data analysis; SZ: study concepts and design, and manuscript editing; SZ, SG: guarantor of integrity of the entire study.

References

1. Martinez MA, Franco S (2020) Therapy implications of hepatitis C virus genetic diversity. Viruses 13: 41. doi: 10.3390/v13010041.
2. Trickey A, Fraser H, Lim AG, Peacock A, Colledge S, Walker JG, Leung J, Grebely J, Larney S, Martin NK, Hickman M,

Degenhardt L, May MT, Vickerman P (2019) The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. Lancet Gastroenterol Hepatol 4: 435-444. doi: 10.1016/S2468-1253(19)30085-8.
3. Smith DB, Bukh J, Kuiken C, Muerhoff AS, Rice CM, Stapleton JT, Simmonds P (2014) Expanded classification of hepatitis C virus into 7 genotypes and 67 subtypes: updated criteria and genotype assignment web resource. Hepatology 59: 318-327. doi: 10.1002/hep.26744.
4. Messina JP, Humphreys I, Flaxman A, Brown A, Cooke GS, Pybus OG, Barnes E (2015) Global distribution and prevalence of hepatitis C virus genotypes. Hepatology 61: 77-87. doi: 10.1002/hep.27259.
5. Petruzziello A, Marigliano S, Loquercio G, Cozzolino A, Cacciapuoti C (2016) Global epidemiology of hepatitis C virus infection: an up-date of the distribution and circulation of hepatitis C virus genotypes. World J Gastroenterol 22: 7824-7840. doi: 10.3748/wjg.v22.i34.7824.
6. Roudot-Thoraval F (2020) Epidemiology of hepatitis C virus infection. Clin Res Hepatol Gastroenterol 45: 101596. doi: 10.1016/j.clinre.2020.101596.
7. Cloherty G, Talal A, Coller K, Steinhart C, Hackett J Jr, Dawson G, Rockstroh J, Feld J (2016) Role of serologic and molecular diagnostic assays in identification and management of hepatitis C virus infection. J Clin Microbiol 54: 265-273. doi: 10.1128/JCM.02407-15.
8. El-Sherif A, Elbahrawy A, Aboelfotoh A, Abdelkarim M, Saied Mohammad AG, Abdallah AM, Mostafa S, Elmestikawy A, Elwassief A, Salah M, Abdelbaseer MA, Abdelwahab KS (2012) High false-negative rate of anti-HCV among Egyptian patients on regular hemodialysis. Hemodial Int 16: 420-427. doi: 10.1111/j.1542-4758.2011.00662.x.
9. Zhang Y, Chen LM, He M (2017) Hepatitis C virus in mainland China with an emphasis on genotype and subtype distribution. Virol J 14: 41. doi: 10.1186/s12985-017-0710-z.
10. Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, Goodman ZD, Koury K, Ling M, Albrecht JK (2001) Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet 358: 958-965. doi: 10.1016/S0140-6736(01)06102-5.
11. Nagamine T, Takagi H, Takayama H, Kojima A, Kakizaki S, Mori M, Nakajima K (2000) Preliminary study of combination therapy with interferon-alpha and zinc in chronic hepatitis C patients with genotype 1b. Biol Trace Elem Res 75: 53-63. doi: 10.1385/BTER:75:1-3:53.
12. Cuypers L, Ceccherini-Silberstein F, Van Laethem K, Li G, Vandamme AM, Rockstroh JK (2016) Impact of HCV genotype on treatment regimens and drug resistance: a snapshot in time. Rev Med Virol 26: 408-434. doi: 10.1002/rmv.1895.
13. Yang XC, Hong ZP, Wang Y, Meng N, Hu Y, Xiong QY, Qin DW, Shen D, Yang XL (2023) Growth history of hepatitis C virus among HIV/HCV co-infected patients in Guizhou province. Front Genet 14: 1171892. doi: 10.3389/fgene.2023.1171892.
14. Szabo SM, Bibby M, Yuan Y, Donato BM, Jiménez-Mendez R, Castañeda-Hernández G, Rodríguez-Torres M, Levy AR (2012) The epidemiologic burden of hepatitis C virus infection in Latin America. Ann Hepatol 11: 623-635. doi: 10.1016/S1665-2681(19)31435-8.
15. Suda G, Ito J, Nagasaka A, Yamamoto Y, Furuya K, Okamoto M, Terashita K, Kobayashi T, Tsunematsu I, Yoshida J, Meguro T, Ohara M, Kawagishi N, Kimura M, Umemura M, Izumi T, Tsukuda Y, Nakai M, Sho T, Natsuizaka M, Morikawa K, Ogawa K, Sakamoto N, NORTE Study Group (2018) Add-on effects of fluvastatin in simeprevir/pegylated-interferon/ribavirin combination therapy for patients with genotype 1 hepatitis C virus infection: a randomized controlled study. Hepatol Res 48: E146-E154. doi: 10.1111/hepr.12938.
16. Magiorkinis G, Magiorkinis E, Paraskevis D, Ho SY, Shapiro B, Pybus OG, Allain JP, Hatzakis A (2009) The global spread of hepatitis C virus 1a and 1b: a phylodynamic and phylogeographic analysis. PLoS Med 6: e1000198. doi: 10.1371/journal.pmed.1000198.
17. Warkad SD, Nimse SB, Song KS, Kim T (2020) Development of a method for screening and genotyping of HCV 1a, 1b, 2, 3, 4, and 6 genotypes. ACS Omega 5: 10794-10799. doi: 10.1021/acsomega.0c00386.
18. Uccellini L, Tseng FC, Monaco A, Shebl FM, Pfeiffer R, Dotrang M, Buckett D, Busch MP, Wang E, Edlin BR, Marincola FM, O'Brien TR (2012) HCV RNA levels in a multiethnic cohort of injection drug users: human genetic, viral and demographic associations. Hepatology 56: 86-94. doi: 10.1002/hep.25652.
19. Kattakuzhy S, Levy R, Rosenthal E, Tang L, Wilson E, Kottilil S (2016) Hepatitis C genotype 3 disease. Hepatol Int 10: 861-870. doi: 10.1007/s12072-016-9748-z.

Corresponding authors

Shan Gao, BS.
Laboratory Medical Center of Lanzhou University Second Hospital, No. 82 Cuiyingmen Lanzhou, Gansu province, P R China.
Tel: 86-09315190363
Fax: 09318458109
Email: gaoshan@lzu.edu.cn

Shangdi Zhang, MS.
Laboratory Medical Center of Lanzhou University Second Hospital, No. 82 Cuiyingmen Lanzhou, Gansu province, P R China.
Tel: 86-09315190363
Fax: 09318458109
Email: zhangsd1985@126.com

Conflict of interests: No conflict of interests is declared.