Prevalence of hepatitis C infection among intravenous drug users in Shanghai

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Abstract

AIM: To characterize the prevalence of hepatitis C virus (HCV) infection among Chinese intravenous drug users (IDUs).

METHODS: A total of 432 adult IDUs (95 women and 337 men) in Shanghai were included in the study. The third-generation Elecsys Anti-HCV assay (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305, Mannheim, Germany) was used to screen for antibodies against HCV. The RIBA strip, a supplemental anti-HCV test with high specificity, was performed on all of the samples that tested positive during the initial screening. All of the anti-HCV positive samples were analyzed with a Cobas TaqMan 48 Analyzer (Roche Diagnostics) for direct detection of HCV RNA. All of the HCV RNA-positive samples were sequenced for genotype determination.

RESULTS: The preliminary screening identified 262 (60.6%) subjects who were seropositive for HCV. Of the 62 females and 200 males seropositive subjects, 16 (16.7%) and 65 (19.3%), respectively, were confirmed by RIBA, yielding an overall HCV seropositive rate of 18.8%. Four female (6.5%) and 14 male (7.0%) subjects tested positive for HCV RNA, indicating an active infection rate of 4.2% for the entire study population. The 18 HCV RNA-positive serum samples were genotyped. Seven individuals were genotype 1b, and four were genotype 1a. One individual each was infected with genotypes 2a, 2b and 3a. Four subjects were co-infected with multiple strains: two with genotypes 1a and 2a, and two with genotypes 1b and 2a. The active infection rate among HCV-seropositive individuals was 22.2%, which was significantly lower than most estimates.

CONCLUSION: The prevalence of HCV is relatively low among IDUs in Shanghai, with a spontaneous recovery rate much higher than previous estimates.

Key words: Hepatitis C; Anti-hepatitis C virus antibodies; Prevalence of hepatitis C virus; Active infection rate; Intravenous drug users

Core tip: In this report, we examined the prevalence of anti-hepatitis C virus (HCV) antibodies, as well as chronic viremia, in 432 intravenous drug users (IDUs) in Shanghai, China. Our data will facilitate the characterization of the prevalence of HCV infection among Chinese IDUs and will complement our understanding of the natural course of HCV infections.

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INTRODUCTION

Hepatitis C virus (HCV) is an enveloped RNA virus with a diameter of approximately 50 nm, and it is classified as a Flavivirus within the Flaviviridae family[2]. Humans are the primary reservoir of HCV; however, the virus has been transmitted experimentally to chimpanzees[3]. The HCV genome consists of a 9.6-kb single-stranded, positive-sense RNA molecule containing one long open reading frame (ORF). This single ORF encodes a large (approximately 3000 amino acids) polyprotein that undergoes co- and post-translational cleavage by host and viral proteases to yield individual viral proteins[2,4]. The N-terminal quarter of the genome encodes core and structural proteins; these proteins consist of a non-glycosylated nucleic acid-binding nucleocapsid protein (core) of 190 amino acids (approximately 21 kDa) and two membrane-associated glycoproteins (E1 and E2/NS1) of 190 and 370 amino acids, respectively (33 and 70 kDa, respectively, when glycosylated). The remaining three-quarters of the genome encode nonstructural proteins NS2-NS5. The NS2 (250 amino acids), NS3 (500 amino acids) and NS4A proteins interact to mediate processing of the presumed NS region of the polyprotein. NS3 is both a proteolytic cleavage enzyme and a helicase, which facilitates unwinding of the viral genome during replication. NS5b is the RNA-dependent RNA polymerase necessary for viral replication[3,4].

Seven HCV genotypes with several distinct subtypes have been identified worldwide[2]. HCV is the etiological agent of hepatitis C. HCV infections are often asymptomatic; however, chronic infection can result in the scarring of the liver, which can ultimately lead to cirrhosis[5,6]. Carriers who develop cirrhosis are at significantly greater risk for developing liver failure, liver cancer or life-threatening esophageal and gastric varices[7]. No effective anti-HCV vaccines are currently available[3,6,9]. The standard of care therapy for patients with HCV infection is the use of both peginterferon and ribavirin. These drugs are administered for either 48 wk (HCV genotypes 1, 4, 5 and 6) or 24 wk (HCV genotypes 2 and 3). These therapies induce a sustained virologic response (SVR) in infected individuals. SVR rates of 40%-50% are observed in patients with genotype 1 infections, and rates of > 80% are observed in those with genotype 2 and 3 infections[8]. Once achieved, SVRs are associated with the long-term clearance of HCV infection, as well as improved morbidity and mortality[9].

Two major advances have occurred in recent years: the development of direct-acting antiviral (DAA) agents; and the identification of several single-nucleotide polymorphisms associated with spontaneous and treatment-induced clearance of HCV infection[11-19]. Although peginterferon and ribavirin remain vital components of therapy, the emergence of DAAs has led to a substantial improvement in SVR rates, along with the option of abbreviated therapy for many patients with genotype 1 chronic HCV infections[8].

The World Health Organization (WHO) estimates that approximately 3% of the global population has been infected with HCV, including more than 170 million chronic carriers at risk of developing liver cirrhosis and/or liver cancer[5]. HCV transmission occurs primarily through exposure to infected blood[5,9]. Specific routes of infection include intravenous drug use, blood transfusions (before 1992), solid organ transplantation from an infected donor, unsafe medical practices, occupational exposure to infected blood, maternal-fetal transmission, sex with an infected person, high-risk sexual practices and possibly intranasal cocaine use[5]. In China, a nationwide HCV serological survey indicated the prevalence of anti-HCV antibodies to be > 0.5% among more than 80000 Chinese subjects. Furthermore, the rates of hepatitis C were much lower than the rates of hepatitis B among clinical inpatient and outpatient populations[20]. Beginning in the early 1990s, the strict screening of blood donors and precise control over the blood supply were implemented by the Chinese government, which effectively eliminated the transmission of many infectious diseases due to blood transfusions. The majority of HCV infections are now limited to specific subpopulations, such as intravenous drug users (IDUs) and patients with certain hemopathies.

Although the prevalence of HCV is greater among IDUs than in the general population, the infection rates of HCV and other diseases remain unknown among IDUs in China. Many hepatologists and virologists worldwide believe that as high as 40%-80% of individuals infected with HCV will develop chronic hepatitis C[22,28]; however, the true rate at which patients develop chronic hepatitis C remains is not known. This gap in understanding regarding the natural course of HCV infection could lead us to misjudge the true burden of HCV infection and might negatively impact clinical decision-making.

In this report, we examined the prevalence of anti-HCV antibodies, as well as chronic viremia, in 432 IDUs in Shanghai, China. Our data will facilitate the characterization of the prevalence of HCV infection among Chinese IDUs and will complement our understanding of the natural course of HCV infections.

MATERIALS AND METHODS

Study population

There are 17 districts in Shanghai, and each district contains one medical center that was established by the local government, where IDUs can receive diaminon therapy for heroin addiction on a regular basis. The total population of Shanghai is approximately 16 million, and Xuhui District is one of the central districts. The residential population of Xuhui District is approximately 1.2 million.
Our samples were collected from Xuhui District. There are approximately 500 IDUs in this district annually, who are treated at the medical center in Xuhui District, where they receive diaminon therapy. A total of 432 adult IDUs, primarily heroin users, were included in this study. Patient serum was collected every 6 mo to monitor HCV, HIV and Treponema pallidum (T. pallidum) subspecies pallidum infections. The participants reported no malaise, weakness, anorexia, jaundice or other symptoms of hepatitis, and they had not previously been diagnosed with viral hepatitis. Accordingly, all of the participants were negative for prior HCV therapy. All of the serum samples used in this study were collected in 2012. Written informed consent was obtained according to the guidelines of the National Ethics Regulation Committee, and the study was approved by the Internal Review Board of the Center for Disease Control and Prevention of Shanghai. The participants were informed of their right to withdraw consent. Consent could be withdrawn by participants, immediate relatives, caregivers or legal guardians.

Screening tests for antibodies to HCV
A third-generation Elecsys Anti-HCV assay (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305, Mannheim, Germany) was used to screen for antibodies against HCV, according to the manufacturer's instructions. The assays were performed using a Cobas 411 e-analyzer. The cutoff index values used for determination of positive reactivity were set based upon the manufacturer's recommendation. Samples with a cutoff-index < 0.9 were considered non-reactive in the Elecsys Anti-HCV assay. Samples having a cutoff-index of ≥ 0.9 and < 1.0 were considered borderline, whereas samples with a cutoff-index of ≥ 1.0 were considered reactive.

Recombinant immunoblot assay
The recombinant immunoblot assay (RIBA) strip, a supplemental anti-HCV test with high specificity, was performed on all of the samples that tested positive during the initial screening. The assays were performed using an MP Diagnostics HCV BLOT 3.0 (MP Biomedicals, Solon, OH, United States), according to the manufacturer's instructions.

Qualitative tests for HCV RNA
A Cobas AmpliPrep Total Nucleic Acid Isolation Kit (Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim, Germany) was used to isolate HCV RNA from serum samples that tested positive for anti-HCV antibodies during the initial screening. Isolation was performed in accordance with the manufacturer's instructions. All of the samples were then analyzed using a Cobas TaqMan 48 analyzer (Roche Diagnostics) for direct detection of HCV RNA.

HCV genotyping
HCV RNA was extracted from 200 µL of EDTA-treated plasma for each HCV RNA-positive sample, using a QIAamp Viral RNA Mini Kit (QIAGEN GmbH, Hilden, Germany), according to the manufacturer's instructions. All of the primers were designed on the basis of consensus sequences, as reported by Duarte et al.[21]. Two sets of primers were designed: one for the 5'-UTR region (for genotypes 1-6), and the other for the NS5B region (supplemental primers for genotypes 1a and 1b). Reverse transcription reactions were conducted with a Reverse Transcription Kit (Biovisualab, Shanghai, China). Multiplex PCR was then performed using a HiFiFast PCR high-fidelity DNA polymerase mix (Biovisualab). PCR was conducted in a Peltier Thermal Cycler (MJ96+/ MJ966) under the following conditions: incubation at 94 °C for 5 min, followed by 35 cycles of denaturation at 94 °C for 10 s; annealing at 58 °C for 30 s; and extension at 72 °C for 30 s. There was then a final extension step at 72 °C for 3 min, and the reactions were held at 4 °C thereafter. For genotype determination, direct sequencing was performed bidirectionally using a Big Dye Terminator Cycle Sequencing Ready Reaction kit (PE Applied Biosystems, Foster City, CA, United States) using 10 ng of QIAquick Spin-purified PCR product (Qiagen) and either the sense or antisense PCR primer, followed by detection on an ABI 310 automated sequencer (PE Applied Biosystems).

Statistical analysis
The results are expressed as the mean ± SD. The statistical analyses were performed using either Student's t-test or analysis of variance with post hoc Scheffe correction when appropriate. P < 0.05 was considered to indicate statistical significance.

RESULTS

Overview of study participants
A total of 432 adult IDUs, ranging from 23 to 63 years of age (mean age 44 ± 9 years old), were enrolled in the study. Of the study participants, 337 were male, and 95 were female. The average history of heroin use was 15 ± 5 years (ranging from 2 to 40 years). The majority of participants administered heroin by injection; all denied sharing syringes. All of the participants were seen at a medical center in Shanghai, where they receive diaminon therapy for heroin addiction on a regular basis. Blood samples were collected every 6 mo to screen for HCV, HIV and T. pallidum infections. The participants reported no malaise, weakness, anorexia, jaundice or other symptoms of hepatitis, and they had not previously been diagnosed with viral hepatitis. Accordingly, all of the participants were negative for prior HCV therapy.

Prevalence of antibodies against HCV
According to recommendations put forth by the United States Centers for Disease Control and Prevention (CDC), the detection of anti-HCV antibodies requires the use of a screening test with high sensitivity. In addition, reactions with low positivity should be verified by RIBA or
PCR to confirm the presence of viral RNA\cite{22,23}.

Preliminary screening tests for HCV were performed using Elecsys assays and a Cobas 411 e-analyzer. Of the 95 females subjects tested, 65.3% were positive for antibodies against HCV. Of the 337 males subjects, 59.3% were positive for antibodies against HCV. No significant differences in infection rates were observed between the men and women. The overall prevalence of anti-HCV antibodies was 60.6%. These results demonstrate a rate of HCV infection among IDUs that is substantially higher than that in the general population.

The sensitivity of the anti-HCV assay was significantly greater than that of the clinical measurements. For the 262 HCV-seropositive individuals, the cutoff index values ranged from 1.6 to 20.1, with an average of 5.7 ± 3.7, well above the standard 1.0 cutoff index value for positive reactivity.

**HCV seropositivity and active infection rates confirmed by RIBA and PCR**

To confirm the presence of viral RNA, we reanalyzed the 262 HCV-seropositive subjects using RIBA and PCR. Of the 62 females and 200 males subjects, 16 (16.7%) and 65 (19.3%) were confirmed to be true positives for anti-HCV antibodies, respectively. Therefore, the true HCV-positive rate of our study subjects was 18.8%. All of the RIBA-positive subjects were seropositive for core proteins. Eight subjects displayed a weak or no reaction to NS3-1, whereas 16 failed to display strong reactivity to NS3-2. Roughly half of the 81 subjects were positive for antibodies against NS4 and NS5.

To determine the current HCV infection rate, the sera from all 262 seropositive individuals were analyzed using the Cobas AmpliPrep/Cobas TaqMan HCV Test. Of the 62 females and 200 males subjects, 4 (6.5%) and 14 (7.0%), respectively, were positive for HCV RNA, indicating an active infection rate of 4.2% for the entire study population.

The 18 HCV RNA-positive sera were then genotyped. Seven individuals were genotype 1b, and four were genotype 1a. One individual each was infected with genotypes 2a, 2b and 3a. Four subjects were co-infected with multiple strains: two subjects with genotypes 1a and 2a, and two subjects with genotypes 1b and 2a.

**HCV infection rates among HCV-seropositive subjects**

HCV remains difficult to both treat and detect due to the high rate of mutation, which severely limits the efficacy of potential vaccines\cite{23}. Current estimates suggest that as many as 70%-90% of infected individuals fail to clear the virus during the acute phase of the disease and therefore become chronic carriers\cite{22,28}. However, the true rate of viral clearance is not known because neither the rate of HCV infection nor the rate of recovery has been established. Some insight into these questions can be drawn from our cohort of IDUs. Of the 16 females and 65 males subjects who tested positive for HCV antibodies, four and 14 subjects were also positive for HCV RNA, respectively (Table 1), yielding an overall clearance rate of 77.8%, which is substantially higher than most estimates\cite{22,23,24,25}.

**DISCUSSION**

Since HCV was identified in 1989\cite{20}, infection by means of blood transfusion has been virtually eliminated worldwide, limiting the spread of HCV to select populations, particularly IDUs\cite{2}. In China, the prevalence of HCV in the general population is relatively low\cite{20}. However, the number of IDUs is increasing, with the spread of numerous infectious diseases, including viral hepatitis, HIV and T. pallidum, subsequently increasing as well. In this report, 18.8% (81/432) of individuals were confirmed to be seropositive for HCV by RIBA testing. Among these individuals, 14 were also positive for HCV RNA, indicating an active infection rate of 4.2% for our cohort. In 1997, the WHO estimated that 3% of the world’s population was infected with HCV\cite{20}; however, a recent nationwide survey in China reported an HCV seropositive rate of <0.5% among more than 80000 Chinese subjects\cite{20}, casting doubt on the WHO estimates. The active infection rate of 4.2% observed in our cohort of IDUs is low compared to other reports; however, it is markedly higher than in the general population. These results highlight the importance of studying at-risk populations, including IDUs.

The active infection rate among HCV-seropositive individuals was 22.2% in this study, which is significantly lower than most estimates\cite{22,23,24,25}. Current estimates suggest that as many as 40%-80% of HCV infections will develop into chronic infections\cite{22,23,24,25}. While these estimates are likely inaccurate, studying infection rates among high-risk populations remains difficult. In addition, the susceptibility and specificity of older detection methods, including anti-HCV and viral RNA tests, are low. The data presented here directly challenge assumptions regarding the rate of chronic infection. Our data indicate that as many as 77.8% of individuals were able to clear HCV infections without the need for anti-viral therapy.

A total of 262 (60.6%) subjects tested positive for anti-HCV antibodies during the initial screening stage, of whom only 81 (18.8%) were confirmed by RIBA, indicating that as many as 181 individuals were false positives detected by the Elecsys and Cobas e-analyzers. The ac-

| Table 1  | Hepatitis C virus current infection rates in anti-HCV positive population |
|----------|-------------------------------------------------------------------------|
|          | NAT(+) | RIBA(+) | NAT(+) / RIBA(+) (%) |
| Female   | 4       | 16      | 25.00%               |
| Male     | 14      | 65      | 21.50%               |
| Total    | 18      | 81      | 22.20%               |

Hepatitis C virus (HCV) current infection rates in anti-HCV positive population were calculated as [number of individuals with nucleic acid testing (NAT)]/total studied population with anti-HCV positive. RIBA: Recombinant immunoblot assay.
The diagnosis of hepatitis is made by biochemical assessment of liver function. Initial laboratory evaluations include total and direct bilirubin, alanine aminotransaminase, aspartate aminotransferase, alkaline phosphatase, prothrombin time, total protein, albumin, globulin, complete blood count and coagulation studies. In this study, we did not perform the above clinical evaluations. Further investigation and follow-up of affected individuals are ongoing.

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REFERENCES

1. Wang Y, Kato N, Jazaz A, Dharel N, Otsuka M, Taniguchi H, Kawabe T, Omata M. Hepatitis C virus core protein is a potent inhibitor of RNA silencing-based antivirus response. Gastroenterology 2006; 130: 883-892 [PMID: 16530526 DOI: 10.1053/j.gastro.2005.12.028]

2. Simmonds P, Bukh J, Combet C, Deléage G, Enomoto N, Feinstone S, Hafion F, Inchauspé G, Kuiken C, Maertens G, Mizokami M, Murphy DG, Okamoto H, Pawlotsky JM, Penin F, Salboung E, Shin T, Stuver Y, Thiel HJ, Viazov S, Weiner AJ, Widell A. Consensus proposals for a unified system of nomenclature of hepatitis C virus genotypes. Hepatology 2005; 42: 962-973 [PMID: 16149085 DOI: 10.1002/ hep.20819]

3. Fraser CS, Doudna JA. Structural and mechanistic insights into hepatitis C viral translation initiation. Nat Rev Microbiol 2007; 5: 29-38 [PMID: 17128284 DOI: 10.1038/nrmicro1598]

4. Moradpour D, Penin F, Rice CM. Replication of hepatitis C virus. Nat Rev Microbiol 2007; 5: 453-463 [PMID: 17487147 DOI: 10.1038/nrmicro1645]

5. Lindenbach BD, Rice CM. Unravelling hepatitis C virus replication from genome to function. Nature 2005; 436: 933-938 [PMID: 16107832 DOI: 10.1038/nature04077]

6. Wang Y, Kato N, Hoshida Y, Yoshida H, Taniguchi H, Goto T, Moriizama M, Otsuka M, Shina S, Shiratori Y, Ito Y, Omata M. Interleukin-1beta gene polymorphisms associated with hepatocellular carcinoma in hepatitis C virus infection. Hepatology 2003; 37: 65-71 [PMID: 12500190 DOI: 10.1053/ jhep.2003.50017]

7. El-Sera H, Epidemiology of viral hepatitis and hepatocellular carcinoma. Gastroenterology 2012; 142: 1264-1273 [PMID: 22537432 DOI: 10.1053/j.gastro.2011]

8. Ghany MG, Nelson DR, Strader DB, Thomas DL, See LF. An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology 2011; 54:

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accuracy of our findings was supported by use of these automated systems, which remove biases caused by human error. Despite improvements in technology, false-positive results for anti-HCV antibodies are a well-known problem. A number of conditions have been shown to induce false positives, including high gamma globulin levels, nephritic syndrome, liver diseases, autoimmune diseases, viral or parasitic infections and pregnancy. The United States CDC estimates that for immunocompetent individuals, approximately 35% of the anti-HCV enzyme linked immunosorbent assay immunosassay results are false positives. Adjustments to cutoff indices have been insufficient to overcome these issues, highlighting the need for more accurate screening methods. Although the third-generation Elecsys Anti-HCV assay and RIBA test detect similar antigens, the RIBA test is capable of distinguishing among the antibodies against core, NS3-1, NS3-2, NS4 and NS5 proteins, and this method was used to confirm the Elecsys results.

Anti-HCV antibodies develop during acute infection, generally between 2 and 8 wk after evidence of liver injury. Anti-HCV antibodies are generally not detectable in patients with initial signs or symptoms of hepatitis C, with some individuals not testing positive until 6-9 mo after the onset of illness. In contrast, hepatitis C viremia can be detected by reverse transcription polymerase chain reaction within a few days after infection. In this study, all of the HCV RNA-positive individuals were confirmed to be seropositive for HCV by RIBA, indicating that the rate of early infection was low.

The 18 HCV RNA-positive sera were genotyped. Seven individuals were genotype 1b, and four were genotype 1a. One individual each was infected with genotypes 2a, 2b and 3a. Four subjects were co-infected with multiple genotypes: two with genotypes 1a and 2a, and two with genotypes 1b and 2a. These data indicate that the genotype distribution in the population is complex.

The diagnosis of hepatitis is made by biochemical assessment of liver function. Initial laboratory evaluations include total and direct bilirubin, alanine aminotransaminase, aspartate aminotransferase, alkaline phosphatase, prothrombin time, total protein, albumin, globulin, complete blood count and coagulation studies. In this study, we did not perform the above clinical evaluations. Further investigation and follow-up of affected individuals are ongoing.

BACKGROUND

Since the discovery of hepatitis C virus (HCV) in 1989, strict screening measures have virtually eliminated viral transmission through blood transfusions, limiting the spread of HCV to select populations, particularly intravenous drug users (IDUs). The prevalence of HCV infection is relatively low among the general population in China. However, infection rates among high-risk populations in China are unknown.

Research frontiers

Many hepatologists and virologists worldwide believe that as high as 40%-80% of individuals infected with HCV will develop chronic hepatitis C; however, the true rate at which patients develop chronic hepatitis C remains is not known. The gap in understanding regarding the natural course of HCV infection could lead us to misjudge the true burden of HCV infection and might negatively impact clinical decision-making.

Innovations and breakthroughs

In this report, the authors examined the prevalence of anti-HCV antibodies, as well as chronic viremia, in 432 IDUs in Shanghai, China. The active infection rate among HCV-seropositive individuals was 22.2%, which was significantly lower than most estimates.

Applications

The data will facilitate the characterization of the prevalence of HCV infection among Chinese IDUs and will complement our understanding of the natural course of HCV infections.

Terminology

The prevalence of anti-HCV antibodies indicates the prevalence of total antibodies against HCV. False positive results for anti-HCV antibodies are a well-known problem. The recombinant immunoblot assay test is capable of distinguishing between antibodies against core, NS3-1, NS3-2, NS4, and NS5 proteins, whereas this method was used to confirm Elecsys results. The active infection of HCV indicates that the HCV RNA could be detected in individual serum by reverse transcription polymerase chain reaction.
Prospects for prophylactic and therapeutic vaccines against the hepatitis C viruses. *Immunol Rev* 2011; 239: 99-108 [PMID: 21198667 DOI: 10.1111/j.1600-065X.2010.00977.x]

Kwo PY, Lawitz EJ, McConne J, Schiff ER, Vierling JM, Poudad D, Davis MN, Galati JS, Gordon SC, Ravendran N, Rossaro L, Anderson FH, Jacobson IM, Rubin R, Koury K, Pedicone LD, Brass CA, Chaudhri E, Albrecht JK. Efficacy of boceprevir, an NS3 protease inhibitor, in combination with peginterferon alfa-2b and ribavirin in treatment-naïve patients with genotype 1 hepatitis C infection (SPRINT-1): an open-label, randomised, multicentre phase 2 trial. *Lancet* 2010; 376: 705-716 [PMID: 20692693 DOI: 10.1016/S0140-6736(10)60934-8]

Poordad F, McConne J, Bacon BR, Bruno S, Manns MP, Sulkowski MS, Jacobson IM, Reddy KR, Goodman ZD, Boparai N, DiNubile MJ, Sniukiene V, Brass CA, Albrecht JK, Bronowicki JP. Telaprevir for previously treated chronic HCV genotype 1 infection. *N Engl J Med* 2011; 364: 1207-1217 [PMID: 21449784 DOI: 10.1056/NEJMoa1000149]

Bacon BR, Gordon SC, Lawitz E, Marcellin P, Vierling JM, Zeuzem S, Poordad F, Goodman ZD, Sings HL, Boparai N, Burroughs M, Brass CA, Albrecht JK, Esteban R. Boceprevir with peginterferon and ribavirin for chronic HCV type 1 infection. *N Engl J Med* 2010; 364: 1195-1206 [PMID: 20692693 DOI: 10.1016/S0140-6736(10)60934-8]

McHutchison JG, Eversen GT, Gordon SC, Jacobson IM, Sulkowski M, Kauffman R, McNair L, Alam J, Muiir AJ. Telaprevir with peginterferon and ribavirin for chronic HCV genotype 1 infection. *N Engl J Med* 2009; 360: 1827-1838 [PMID: 19403902 DOI: 10.1056/NEJMoa0806104]

Hézode C, Forestier N, Dasheiko G, Ferenci P, Pol S, Goeser T, Bronowicki JP, Bourlière M, Gharakhaniyan S, Bengtsson L, McNair L, George S, Kieffer T, Kwong A, Kaufmann RS, Alam J, Pavlotsky JM, Zeuzem S. Telaprevir and peginterferon with or without ribavirin for chronic HCV infection. *N Engl J Med* 2009; 360: 1839-1850 [PMID: 19403903 DOI: 10.1056/NEJMoa0807650]

Jacobson IM, McHutchison JG, Dasheiko G, Di Bisceglie AM, Reddy KR, Bzowey NH, Marcellin P, Muiir AJ, Ferenci P, Flisiak R, George J, Rizzetto M, Shouval D, Sola R, Terg RA, Yoshida EM, Adda N, Bengtsson L, Sankoh AJ, Kieffer TL, George S, Kaufmann RS, Zeuzem S. Telaprevir for previously untreated chronic hepatitis C virus infection. *N Engl J Med* 2011; 364: 2405-2416 [PMID: 21696307 DOI: 10.1056/NEJMoa1012912]

Zeuzem S, Androune P, Pol S, Lawitz E, Diago M, Roberts S, Focaccia R, Younossi Z, Foster GR, Horban A, Ferenci P, Nevens F, Müllhaupt B, Pockros P, Terg R, Shouval D, van Hoek B, Weiland O, Van Heeswijk R, De Meyer S, Luo D, Boogaerts G, Polo R, Picchio G, Beumont M. Telaprevir for retreatment of HCV infection. *N Engl J Med* 2011; 364: 2417-2428 [PMID: 21696308 DOI: 10.1056/NEJMoa1013086]

Thomas DL, Thio CL, Martin MP, Qi Y, Ge D, O’Huigin C, Kidd J, Kidd K, Khakoo S, Alexander G, Goedert J, Kirk GD, Donfield SM, Rosen HR, Tobler LH, Busch MP, McHutchison JG, Goldstein DB, Carrington M. Genetic variation in IL28B and spontaneous clearance of hepatitis C virus. *Nature* 2009; 461: 798-801 [PMID: 19759553 DOI: 10.1038/nature08463]

Ge D, Fellay J, Thompson AJ, Simon JS, Shianna KV, Urban TJ, Heinenz EL, Qu P, Bertelsen AH, Muiir AJ, Sulkowski M, McHutchison JG, Goldstein DB. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. *Nature* 2009; 461: 599-601 [PMID: 19684573 DOI: 10.1038/nature08309]

Lu J, Zhou Y, Lin X, Jiang Y, Tian R, Zhang Y, Wu J, Zhang F, Zhang Y, Wang Y, Bi S. General epidemiological parameters of viral hepatitis A, B, C, and E in six regions of China: a cross-sectional study in 2007. *PloS One* 2009; 4: e8467 [PMID: 20041146 DOI: 10.1371/journal.pone.0008467]

Duarte CA, Foti L, Nakatani SM, Riediger IN, Poersch CO, Pavoni DP, Krieger MA. A novel hepatitis C virus genotyping method based on liquid microarray. *PloS One* 2010; 5: [PMID: 20862224 DOI: 10.1371/journal.pone.0012822]

Reference for Interpretation of Hepatitis C Virus (HCV) Test Results. Available from: URL: http://www.cdc.gov/hepatitis

Hepatitis C Virus (HCV) Infection Testing for Diagnosis. Available from: URL: http://www.cdc.gov/hepatitis

EASL International Consensus Conference on hepatitis C. Paris, 26-27 February 1999. Consensus statement. *J Hepatol* 1999; 31 Suppl 1: 3-8 [PMID: 10622553]

Lemon SM. Brown EA. Hepatitis C virus. In: Mandell GL, Bennett JE, Dolin R, editors. Principle and Practice of Infectious Disease. 4th ed. New York: Churchill Livingstone, 1995: 1474-1486

Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a DNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* 1989; 244: 359-362 [PMID: 2523562]

Watson JM, Stallcup P, Escamilla D, Chernay P, Reyes A, Trevino SC. Evaluation of the Ortho-Clinical Diagnostics Virostecs ECI Anti-HCV test: comparison with other methods. *J Clin Lab Anal* 2007; 21: 162-166 [PMID: 17506481 DOI: 10.1002/jcla.20119]

Pereira FM, Bertollo LA, Zarife MAS. Comparison of two automated chemiluminescence tests for the detection of antibodies against the hepatitis C virus. *Rev Pan-Amaz Saude* 2010; 1: 17-21 [DOI: 10.5123/S2176-62232010004000003]
