Original Article

Diversity of Genotype and Mode of Spread of Hepatitis C Virus in Northern India

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ABSTRACT

Background/Aim: Hepatitis C is caused by hepatitis C virus (HCV), which is classified into 6 genotypes. It leads to chronic hepatitis in 80% of the cases. Genotype of the virus helps in predicting response to antiviral therapy and also the duration of treatment. Therefore, it is important to know the prevalence of each genotype. Knowledge regarding the route of entry of HCV in the blood is also necessary to formulate a strategy to prevent its spread. **Patients and Methods**: One hundred and two newly diagnosed patients with chronic hepatitis C, having anti-HCV antibody-positive were included in the study. Their HCV RNA viral load and genotype were determined by Reverse Transcriptase PCR assay on Roche Cobas Ampliprep analyzer. **Results**: Genotype 3 was commonly detected in 58.8% patients followed by genotype 1 in 20.6%. Twelve patients had genotype 4 (11.8%) and 9 had mixed infection with genotypes 3 and 4. Among these patients, 43.1% of patients had a history of multiple injection exposure. Blood transfusion received by 6.9% and 2.9% had donated blood. Only 1 patient had a history of drug abuse. **Conclusion**: The distribution of genotypes varies in different regions and therefore its knowledge is important, as it determines the response of the patient to the treatment. The use of autodisabled syringes, their proper disposal, following biomedical waste management guidelines, and organizing continued medical education and workshops will help in preventing the spread of HCV infection.

Key Words: Genotype, hepatitis C virus, Northern India, prevalence

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Hepatitis C is caused by a spherical, enveloped, single-stranded RNA virus, which belongs to the family Flavivirdae and genus Flavivirus. It is a major cause of chronic hepatitis C, throughout the world. WHO estimates that 170 million individuals worldwide are infected with hepatitis C virus (HCV). However, the prevalence of HCV infection varies throughout the world.[1]

HCV is classified into 6 genotypes and numerous subtypes. Molecular differences between the genotypes are relatively large and have a difference of at least 30% at the nucleotide level. The viral genome undergoes mutation and thus the parent strain has different mutants, which coexist as quasispecies in the same individual.[2]

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HCV leads to chronic hepatitis in about 80% of the cases.[3] The virus can cause gradual hepatic fibrosis and eventual cirrhosis, end-stage liver disease, and hepatocellular carcinoma.[4] Without treatment, the expected time to develop cirrhosis is less than 20 years.[5]

The virus genotype does not influence the presentation of the disease but different strains of HCV may be involved in the disparity in the course of the hepatitis C among infected individuals and difference in the pattern of the disease between countries with different dominant genotypes.

Since it is a major predictor of response to antiviral therapy and also determines the duration of treatment, it is important to understand the prevalence of the type of genotype to device strategies to combat and to take preventive measures. It is also important to understand the route of entry of HCV in the blood so that its spread can be prevented, therefore the study was planned to know the genotype and its probable mode of transmission.

PATIENTS AND METHODS

One hundred and two newly diagnosed patients with chronic hepatitis C infection, who attended the Medicine outpatient clinics at the Lady Hardinge Medical College (LHMC) and associated Smt. SSK Hospital, New Delhi, during 2007–2009, between 18 and 60 years of age were included in this prospective study. The study protocol was approved by the Institutional Ethics Committee, LHMC. A written informed consent was taken from all the patients. A detailed clinical history of the patient, including past history of taking multiple injections, blood donation, blood transfusion, and drug abuse, was taken and recorded in the patient case record by the treating physician.

All the patients had anti-HCV antibody-positive test done by ELISA (Tri Dot) test. HCV RNA viral load and genotype was done for all the patients before starting the combination therapy with injection Interferon-α2a thrice weekly subcutaneously and capsule ribavirin 1000 mg orally. HCV RNA quantitative test was done by Reverse Transcriptase PCR assay on Roche Cobas Ampliprep analyzer (Roche Diagnostics GmbH, Mannheim, Germany), ranging from 43 IU/mL to 6.9×10^7 IU/mL. A viral count of <43 IU/mL was considered to be undetectable.

RESULTS

The characteristics of the study patients are shown in Table 1. Commonly detected genotype of HCV was genotype 3 (58.8%) followed by genotype 1 (20.6%). Twelve patients (11.8%) showed infection with genotype 4 and 9 (8.2%) patients had mixed infection with both 3 and 4 genotypes.

Among 102 patients with HCV infection, 44 (43.1%) patients had a history of multiple injection exposures, 7 (6.9%) patients had blood transfusion, and 3 (2.9%) patients had a history of donating blood. Only 1 patient was an intravenous (IV) drug abuser.

Table 1: Characteristics of the study patients (n = 102)

Parameter studied	
Mean age of the patients (years)	34.6 ± 10.3
Gender [No. (%)]	
Male	79 (77.5%)
Female	23 (22.5%)
Mean weight of the patients (kg)	57.3 ± 5.9

DISCUSSION

Hepatitis C infection is the most common cause of chronic liver disease. The severity of hepatitis C, its progression, and response to therapy may vary depending on the genotype.[6]

As regional differences exist in the distribution of HCV genotype,[7] it is important to know the genotype distribution to understand its prognostic implication. In our study, genotype 3 was predominant, which is similar to that reported by other workers from Western and Northern India.[8-13] In Southern India, genotype 1 was found to be predominant,[14] whereas it was second commonly detected in our study. In the United States, HCV genotype 1 accounted for the majority (74%) of infections followed by genotype 2 (15%), genotype 3 (6%), and genotype 4 (1%).[15,16]

The common modes of transmission of hepatitis C infection are blood transfusion, IV drug use, unsafe therapeutic injection, and health care-related procedures.[17] In the developed countries, the main route of hepatitis C infection is IV drug abuse, whereas in India blood transfusion and unsafe injection practices are predominant modes of hepatitis C transmission.[17] Blood transfusion is a major mode of transmission of HCV, as a large quantity of virion enters the patient. This mode of transmission should be controlled. In our study group, 6.9% of HCV patients received blood transfusion.

In India, the prevalence of HCV infection in thalassemic patients has been reported to be 21%[18] and in 26.6% children with varied diagnosis who received multiple blood transfusions.[19]

The prevalence of hepatitis C in healthy blood donors was reported to be 1.09% in Punjab, India,[20] and 87.3% in commercial blood donors in Maharashtra, India.[21] Studies have shown prevalence of hepatitis C to be below 2% in voluntary donors.[22-24] In Nigeria, commercial donors constitute 63% of donor population. Commercial donors had high prevalence of HCV infection (80%) than voluntary donors (5%).[25] In our study, the prevalence of hepatitis C was 2.9% in blood donors. The reason for this high prevalence may be for the reason that in India mandatory screening of blood and blood products was introduced only in 2002, whereas in the United States, mandatory screening of blood was introduced in 1990. After this mandatory screening, the prevalence of hepatitis C in the United States reduced from 3.84% to 0.5%.[26]

It is important to screen the blood donors in India to control the spread of HCV infection. In India in blood banks, blood is screened for HIV, Hepatitis B surface Antigen, HCV, malaria, and syphilis as per Drugs and Cosmetic rules before sending for blood transfusion to the patients.[27] The latest specific measure is the introduction of viral nucleic acid test (NAT). NAT screening is currently in use in most of the developed countries, such as the United States, Brazil, Canada,

Australia, New Zealand, Japan, Singapore, Indonesia, and Malaysia. NAT is not yet mandatory in India. The NAT system, which was approved for use in 2002 by the FDA, can detect HIV and HCV infections in blood donors earlier than other screening tests because it detects viral genes rather than antibodies or antigens. The appearance of antibodies requires time for the donor to develop an immune response, and the detection of antigens requires time for a higher level of virus to appear in the bloodstream. With the use of NAT for HCV, the window period is reduced by approximately 60 days (from an average of 70 days to 10 days) during which a donor can be infected, but have negative screening tests.[28]

In India paid blood donation is illegal, and there is no strong monitoring or expert donor counseling in many blood banks. Most of the blood banks use serologic screening methods for screening of the infections. Most of these serologic tests are not sensitive enough and very few blood banks use the more sensitive third- or fourth-generation Enzyme immunoassay tests to screen the viral markers. Increased voluntary donation, availability of safe blood, component preparation, and optimum utilization of blood products are the key needs. To assure blood safety, mandatory NAT screening should also be implemented in India.

In our study 9 patients (8.2%) had mixed infection with both genotypes 3 and 4, which was lower than that reported by a study in Egypt in 2009 where 34.28% patients were infected with genotypes 3and4.[29]

In the present study only 1 patient revealed the history of drug abuse who belonged to North East region of the country, where the prevalence of HCV infection has been reported to be 92% in IV drug abuser.[30] The patients might not have disclosed their drug abuse habit due to the stigma of drug addiction or fear of refusal of treatment from physicians.

In our study, 43.1% of hepatitis C patients had a history of multiple exposures to injections from local practitioners. The excessive use of injections is common in the developing countries. Rehan *et al*. (1998) reported in the drug utilization study in Nepal that about 50% of all the drugs prescribed were administered by injection.[31] People in rural areas in the developing countries have a myth that injections have more healing power.[31] Considering this it appears that inappropriate injection practices among the health care providers could also be the possible reason for the spread of HCV infections.

Continued medical education regarding reinforcing good injection practices for health care providers, use of autodisabled syringes, proper disposal of used syringes and needles, and/or adequate screening of the blood may be the solution for the prevention of further transmission of HCV infection.

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