Genotypic Distribution and Associated Disease Pattern of Hepatitis C Virus in Northern India

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ABSTRACT

Background & Objectives : Hepatitis C virus (HCV) genotype has emerged as an independent factor for disease progression, and it also influences the duration and response to anti-viral therapy. HCV genotypic distribution varies geographically. This retrospective analysis was performed to study the genotypic distribution of chronic hepatitis C and its effect on disease presentation in northern Indian population.

Material and Methods: All treatment eligible patients with HCV infection presenting to the gastroenterology out-patient department at our institute between January 2004 and December 2013 were enrolled.

Results: A total of 1202 patients with hepatitis C virus infection were included. The mean age of patients was 41.5 ±11.8 years and 70% were males. The mean ALT level was 106.4 ± 85.4 IU/L and high viral load was present in 50.7%. Evidence of cirrhosis was present in 22.5%. The most common genotype was genotype 3 (80.1%), followed by genotype 1 (15.4%), genotype 4 (1.4%) and genotype 2 (0.5%). All the clinical and biochemical characteristics in genotype 1 and 3 patients were similar except that a significantly higher proportion of patients with genotype 1 had a high viral load. The percentage of cirrhotic patients among genotype 1 was 25.9% as compared to 22.2% among genotype 3.

Interpretation & Conclusion: Genotype 3 is the most prevalent genotype in the HCV infected patients in northern India, followed by genotype 1. There was no significant difference in disease presentation among genotype 1 and 3 patients.

Keywords: Hepatitis C virus, genotype

IINTRODUCTION

Chronic infection with hepatitis C virus (HCV) is a major public health problem, which has affected about 180 million people infected worldwide. Natural history studies report that around 20%-30% of patients with chronic hepatitis C (CHC) will eventually develop clinical complications such as cirrhosis, liver decompensation and hepatocellular carcinoma.[1]

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Progression of HCV related liver disease is influenced by various factors such as viral genotype, viral load, duration of infection, age of infection, body weight, alcohol consumption, and concurrent infection by hepatitis B virus (HBV) or human imunodeficiency virus (HIV).[2] Out of these, HCV genotype has emerged as an independent factor for disease progression, which also influences the duration and response to anti-viral therapy.[3]

HCV genotype is defined as genetic heterogeneity among different HCV isolates with 66%–69% nucleotide homology, while subtype is referred as closely related isolates within each of the major genotypes with a 77%–80% nucleotide homology.[4] The prevalence of HCV genotypes varies geographically. Six HCV genotypes, numbered 1–6, and a large number of subtypes have been described. Genotype 1 (subtypes 1a

and 1b) is by far the most prevalent genotype worldwide, with a higher prevalence of 1b in Europe and 1a in the US. Genotype 3a is highly prevalent in European intravenous drug users.[5] This group is currently experiencing an increasing incidence and prevalence of infections related to HCV genotype 4. Genotype 2 is found in clusters in the Mediterranean region, while 5 and 6 are rarely found.[6] Most of the Indian studies report predominance of genotype 3, while some studies from Southern India have reported genotype 1 to be common.[2,7-12] We performed this retrospective analysis to study the genotypic distribution of chronic hepatitis C and its effect on disease presentation in northern Indian population.

MATERIAL AND METHODS

All treatment eligible patients in age group of 18-70yrs with HCV RNA postivity (chronic hepatitis or compensated cirrhosis) presenting to the gastroenterology out-patient department at our institute between January 2004 and December 2013 were enrolled. Patients who had co-infections with HBV or HIV viruses were excluded.

A detailed history and clinical examination was undertaken. Baseline laboratory work-up included haemogram, liver and renal function tests, thyroid function tests, prothrombin time index (PTI), fasting blood sugar, α-feto protein and ultrasound abdomen. Cirrhosis was diagnosed on the basis of clinical, laboratory, radiological, endoscopic and/or histological criteria (where available). Increased alanine aminotransferase (ALT) was defined as ALT levels >40 IU/L. Liver biopsy for genotype 1 and 4 patients, and/or elastography measurement (year 2008 onwards) were done where indicated. All the patients were tested for HBsAg and HIV co-infections.

Anti-HCV antibody positivity was confirmed by ELISA (ELISCAN HCV; RFCL limited, Dehradun, India). HCV Ribo-Nucleic Acid (RNA) was quantified by real time polymerase chain reaction technology (COBAS Taqman HCV TEST 2.0; Roche Diagnostics Corporation, Indiapolis, IN, USA). High viral load was defined as HCV RNA >4,00,000 IU/ml.

HCV Genotype was determined using the following method- HCV RNA was extracted from plasma or serum samples using QiaSymphony DSP Virus/pathogen kit on the Qiagen Qiasymphony platform. The Extracted RNA was used for reverse-transcription-amplification by utilizing the one-step RT-PCR enzyme AgPath ID from Invitrogen. The target region for genotyping was selected as aprox 245 bp region of the 5'UTR. Sequencing was performed on ABI 3500DX system using BDT 1.1. The genotype was elucidated by posting the sequences into the HCV database (Los Alamos National Laboratory; http.hcv.lanl.gov/content/sequence/ Basic_Blast/basic_blast.html).

Continuous data were expressed as means ±SD. Categorical data were expressed as number/proportion of subjects with a specific feature. Chi-square test was used to compare categorical data. A two-tailed p value of less than 0.05 was required for statistical significance.

RESULTS

A total of 1202 patients with hepatitis C virus infection were included in this retrospective analysis. Patients with co-infections or in whom genotype was not available were excluded. The mean age of patients was 41.5 ±11.8 years and 70% were males.

The mean ALT level was 106.4 ± 85.4 IU/L with a range of 14–645 IU/L. Evidence of cirrhosis was present in 22.5% (n=270). High viral load (HCV RNA > 400,000 IU/ml) was present in 50.7% (n=602). The genotypic distribution of patients is shown in Figure I. The most common genotype was genotype 3 (80.1%) followed by genotype 1 (15.4%) and other genotypes (4.5%).

Comparison between clinical and biochemical characteristics of genotype 1 and 3 patients is shown in Table I. All the characteristics were similar in both the

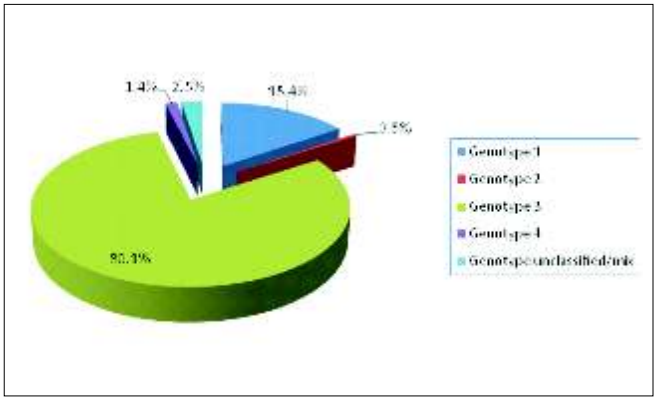

Fig. I: Distribution of various HCV genotypes

Table I

Comparison of characteristics of genotype 1 and 3 chronic hepatitis C patients

Parameter	Genotype 1 (n=185)	Genotype 3 (n=963)	p value
Age (years)	40.6 ± 11.4	41.7 ± 12.0	0.25
Males (%)	71.4%	69.5%	0.881
Weight (kg)	66.9 ± 12.3	72.2 ± 12.1	0.341
BMI	23.8 ± 3.9	24.4 ± 4.3	0.768
ALT (IU/L)	101.1 ± 76.7	107.6 ± 93.5	0.55
ALT >40 IU/L	87.6%	86.2%	0.668
HCV RNA >4,00,000 IU/ml	75.1%	48.3%	0.0001
Presence of cirrhosis	25.9%	22.2%	0.853
Presence of any co-morbid condition	10.8%	13.7%	0.692
Presence of Diabetes Mellitus	8.6%	10.2%	0.593
Past history of alcohol use	18.9%	14.6%	0.148

Data is expressed as mean ± S.D. or percentage (number)
ALT, Alanine transaminase; AST, Aspartate transaminase; BMI, Body mass index; HCV RNA Hepatitis C virus ribonucleic acid

subgroups except that a significantly higher proportion of patients with genotype 1 had a high viral load (HCV RNA >4,00,000 IU/ml). The percentage of cirrhotics among genotype 1 patients was 25.9% compared to 22.2% among genotype 3 patients.

DISCUSSION

The present study, carried out on a large group of patients in a tertiary care hospital, clearly demonstrates that genotype 3 is the commonest HCV genotype in northern India. This data is in concordance with other data published from the Indian subcontinent in the general population suggesting a higher prevalence of HCV genotype 3 in India. Genotype 1 was found to be the second most common genotype. Other rare genotypes were genotypes 2 and 4.

There are several reports on the prevalence of different HCV genotypes from India. In the studies from Northern, Eastern as well as Western region, genotype 3 has been predominant,[2,7-10] while in Southern India, genotypes 1 and 3 have been reported in decreasing order of frequency. HCV genotype 4 and 6 have been reported exclusively from South India.[11,12]

The correlation of HCV genotype with the severity of liver disease is still controversial. Studies suggested that HCV genotype 1 leads to a more severe course and appear to be associated with distinct manifestations of the liver disease.[13] On the contrary, other studies reported that HCV genotypes do not have a significant effect on the severity and outcome of liver disease.[14] In our study, we found that the severity of liver disease at presentation in patients infected with genotypes 1 and 3 was not significantly different. Although patients infected with HCV genotype 1 had a greater viral load compared to those with genotype 3 infection, the proportion of patients having cirrhosis, and the transaminase levels at presentation were not significantly different in the two groups.

The correlation of HCV genotype with steatosis is again a controversial issue and varies from population to population. It has been proposed that HCV may alter directly the lipid metabolism with an accumulation of triglyceride-rich lipid droplets within the cytoplasm of hepatocytes. Several studies have reported fatty changes in the liver in 30% to 70% of patients with chronic hepatitis C. A European study suggested that HCV genotype 3 is associated with higher steatosis scores than in other genotypes.[15] In one study from India, steatosis was found in 70% of liver biopsy samples from chronic hepatitis C patients.[16] However, we did not study this

aspect in our study.

In conclusion, this study provides a large data base for HCV infected patients from India. Our study clearly shows that genotype 3 is the most prevalent genotype in the HCV infected patients in northern India, followed by genotype 1. There was no significant difference in disease presentation among genotype 1 and 3 patients.

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