

HCV Genotype 2 is Rare in India - Ten Years' Experience at Tertiary Care Center of Northern India

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1. Abstract

1.1. Introduction: Viral hepatitis is an important health problem in India and is caused by Hepatitis A, B, C, D, E and G virus which can lead to acute or chronic infection.

1.2. Aims & Objectives: To determine the genotype of chronic hepatitis C patients attending Department of Gastroenterology, PGIMS Rohtak.

1.3. Summary and Conclusions: Our study highlights that Genotype 2 is rare in India and Genotype 3 is most common genotype which is difficult to treat Genotype with oral antiviral therapy.

2. Introduction

Viral hepatitis is recognized as a public health problem in India and globally. Various etiological agents (Hepatitis A, B, C, D, E and G virus) have been implicated that can lead to acute, chronic or acute on chronic infection. While Hepatitis A and E are often the cause of sporadic outbreaks of hepatitis, Hepatitis B and C can either clear spontaneously or can lead to chronic infection and thereafter sequel like cirrhosis and Hepatocellular Carcinoma (HCC) [1].

Hepatitis C Virus (HCV) is one of the major cause of death and morbidity and recent estimates showed Seroprevalence of 2.8%, corresponding to greater than 185 million infections worldwide.²In India there are about 6-12 million people with HCV infection with a mortality of 37,000 deaths in the year 2015 [1].

HCV is a single-stranded, positive sense RNA virus belonging to family *Flaviviridae* and genus *Hepacivirus*. There are six distinct major

genotypes (genotype 1 to 6) and a minor genotype 7. As the HCV virus replicates rapidly, it constantly changes and mutates thus making it difficult to develop vaccine against HCV [3].

Genotyping is useful for investigating outbreaks, for understanding the epidemiology and virological features of this virus, for correct stratification of groups and accurate analysis of data related to efficacy and resistance of new HCV drugs. It is also essential for the implementation of therapeutic procedures, the production of effective vaccines, and the improvement of diagnostic tests [3]. A recent study shows that HCV genotypes 1 and 3 are the two most prevalent genotypes in India and globally, and account for about 76.3% cases of HCV in the world [4].

HCV infection is usually acquired through infected syringes and needles, and transfusion of infected blood. Sexual transmission of HCV occurs infrequently in heterosexual couples. It is reported to be more common in HIV-positive persons, particularly in high risk group of male having sex with male (MSM). The risk of transmission of HCV from a mother to her child occurs in 4–8% of births to women with HCV infection, and in 10.8–25% of births to women with HIV and HCV co-infection. HCV causes both acute and chronic hepatitis. Acute hepatitis is often clinically mild and marked by fluctuating elevations of serum aminotransferase levels; >50% likelihood of chronicity, leading to cirrhosis in >20% [5].

Chronic infection with HCV is usually clinically silent, and is only very rarely associated with life-threatening disease. Spontaneous clearance of acute HCV infection occurs within six months of infec-

tion in 15–45% of infected individuals in the absence of treatment. Almost all the remaining 60–80% of persons will harbor HCV for the rest of their lives (if not treated) and are considered to have chronic HCV infection. Left untreated, chronic HCV infection can cause liver cirrhosis, liver failure and HCC. Of those with chronic HCV infection, the risk of cirrhosis of the liver is 15–30% within 20 years. The risk of HCC in persons with cirrhosis is approximately 2–4% per year [6].

Currently highly effective DAAs have however changed the HCV treatment paradigm, leading to hope of elimination of this infection as a public health threat by the year 2030. WHO introduced global targets for the care and management of HCV including “a 90% reduction in new cases of chronic hepatitis C, a 65% reduction in hepatitis C deaths, and treatment of 80% of eligible people with chronic hepatitis C infection [7]. DAAs are the recommended first line treatment in India.

3. Review of Literature

In 2016, Petruzzello A *et al* conducted a systematic study to quantify global HCV epidemiology, using the best available published data between 2000 and 2015 from 138 countries. Total global HCV prevalence was estimated to be 2.5% (177.5 million of HCV infected adults), ranging from 2.9% in Africa and 1.3% in Americas. HCV genotype 1 was the most prevalent worldwide genotype (49.1%), followed by genotype 3 (17.9%), 4 (16.8%) and 2 (11.0%). Genotypes 5 and 6 were observed to be responsible for the remaining < 5% of

the study population [2].

In a study conducted by Samir R S *et al*, the prevalence of HCV genotypes and subtypes in different geographic regions of India was assessed among 500 patients and they observed that genotype 3 was the most common genotype overall (54%) followed by genotype 1 (24%) and genotype 4 (6%) [4].

An observational study was conducted by B. Debjyoti *et al* among 350 chronic liver disease patients, 110 were positive for anti-HCV antibodies and on further confirmation, 66% patients were found to be HCV RNA positive. In them, Genotype 3 was found to be most common genotype positive in 48 (73%) patients, of these 44 patients (67%) and Genotype 1a was seen in 18 (27%) patients [8].

Chakravarti A *et al* followed Fifty four anti-HCV positive patients, in which 31 were positive for HCV RNA. Genotype 3 was found to be the commonest genotype present in all risk groups followed by type 1. Genotype 1 was associated with a significantly higher viral load as compared to genotype 3 [9].

A study was conducted by Verma R *et al* in the year 2012 to determine the incidence of HCV infection in the Ratia block of the Featherbed district, Haryana, India. From a total of 7533 samples, anti-HCV Abs were found to be positive in 25.3% (1912/7533) cases by using ELISA test. This was the first and the largest government-aided study to be conducted in Haryana state of India, with important observations that there were some highly endemic areas in Haryana for HCV infection with a very high prevalence [10].

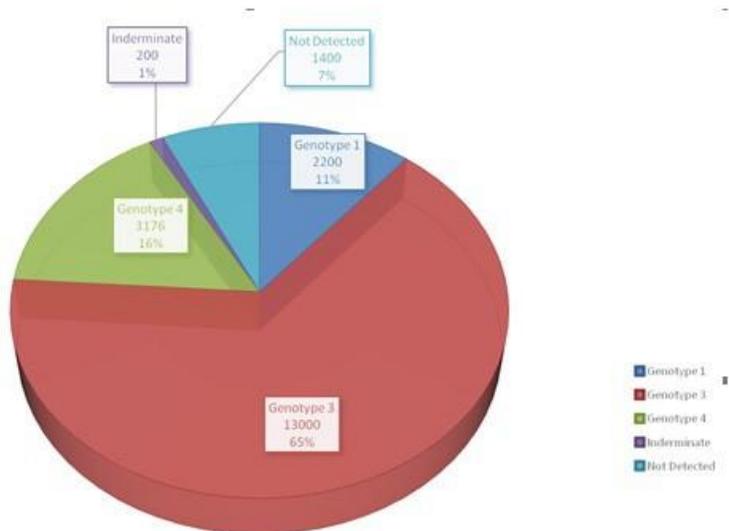


Figure 1: Chart Showing Analysis of Genotype in Twenty Thousand Patients

4. Aim & Objective

To determine the genotyping of HCV infections among chronic hepatitis patients attending Department of Gastroenterology, PGIMS Rohtak.

5. Material and Methods

The present study was undertaken in department of Gastroenter-

ology, PGIMS (Rohtak), over a time period of ten years i.e. from 01.09.2010 to 31.08.2020. A total of 20,000 Anti HCV-Ab positive patients were included in this study. Patients who gave informed consent to participate in the study were enrolled. Then 5 ml of blood sample of these patients were collected by venipuncture in vacutainer (red capped) after taking all aseptic measures [11]. The serum was

then subjected to ELISA for HCV antibody detection using HCV-Ab ELISA kit. The samples positive for anti-HCV Ab were further tested by real time-polymerase chain reaction (rt-PCR) test for molecular confirmation and genotyping. HCV RNAs from the serum sample were extracted, then subjected to rt-PCR test. Viral load of the samples was assessed using HCV rt-PCR kit. The samples positive for HCV-RNA by rt-PCR were further tested for genotyping of HCV using HCV genotyping kit. All the biomedical waste generated during this study in the laboratory was discarded after proper disinfection or sterilization as per the Biomedical Waste Management and Handling rules 2016 guidelines, and Bio-Medical Waste Management (Amendment) Rules 2018 [12-13].

6. Observations & Results

All the twenty thousand patients who were found to be Anti HCV Antibody positive and after informed consent gave blood samples for baseline HCV RNA Quantitative and Genotyping.

Out of total of ten thousand patients, most common Genotype was 3 which was seen in 65% (13,000 patients) followed by Genotype 4 which was present in 15.88% (3176 patients). Genotype 1 was seen in 11% (2200 patients), Genotype 5 was seen in 0.06% (12 patients), Genotype 6 in 0.05% (10 patients) and Genotype 2 in 0.01% (2 patients) and the proportion is so negligible that even it cannot be depicted on above pie chart showing distribution of genotypes in ten thousand patients. The Genotype could not found to be in 1% (200 patients) due to low viral load i.e. Indeterminate group. There were 7% (1400 patients) in whom baseline HCV RNA Quantitative, no virus was found and hence Genotype test was also negative.

It has been already reported that in India there is North- South divide i.e. Genotype 3 is predominant in North India whereas Genotype 1 & 4 is common in South India. Our study also confirms the same but normally in North India Genotype 1 is more common than Genotype 4 but in our study it is reverse and majority of patients belonging to Genotype 4.

7. Conclusions

Our study clearly highlights that Genotype 2 is rare in India and Genotype 3 is most common genotype which is difficult to treat Genotype with oral antiviral therapy.

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