

Genotype-8: A Modern Family Member of Hepatitis C Virus

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ABSTRACT

Hepatitis C Virus (HCV) is a highly diverse and pervasive disease around the globe, with a prevalence ranging from 1.5 to 2.3%. With wide genetic variability, it is classified into seven Genotypes (GT) with 67 subtypes. The sighting of a modern HCV GT-8 ratifies its endemic character in India, particularly in the Punjab State. Getting familiarized and making aware of the HCV genotypes and subtypes is necessarily essential in establishing the optimal treatment regimen.

Key words: Hepatitis C, RNA virus, Epidemiology, Genotype Classification, Genotype 8, India.

INTRODUCTION

Hepatitis C Virus (HCV) is a single-stranded RNA virus which belongs to the genus Hepacivirus of family Flaviviridae and was discovered for the very first time in the year 1989.¹ It acts as a major cause for Chronic Liver Disease (CLD), Cirrhosis and Hepato-Cellular Carcinoma (HCC).² HCV can be transmitted through various routes, which includes the direct contact with the infected blood and body fluids, invasive medical procedures, i.e., surgery, body tattooing, IV drug abuse and sexual intercourse.³ HCV was categorized into seven genotypes with 67 subtypes until the discovery of genotype 8.⁴ The identification of novel genotype eight has added 17 subtypes to the family of HCV, which make up the total to 8 genotypes with 84 subtypes.⁵

Epidemiology

Among the different types of Hepatitis, HCV is considered as the leading cause of morbidity and mortality across the world. Since the past two decades, the global mortality of HCV has inclined from 0.89 million to 1.45 million and emerged as the seventh

leading cause of death worldwide.⁴ When it comes to the deaths related to HCV, the continents like Asia and Africa are predominantly affected than other continents (≥ 33.50 deaths per 100,000 population per year). In particular, there observed 52% higher deaths in east and south Asia.⁶ Unlike the other communicable diseases which prevalently occur in low-income countries, Hepatitis is highly endemic in middle and high-income countries. As HCV is chronic and life-long infection, it could progress in liver damage, which leads to cirrhosis and hepatocellular carcinoma.

HCV in Indian Context

The findings from a recent systematic review infer that the prevalence of HCV infected adults globally is 2.5% and 64.4% viraemic load in Asia.⁵ Among the HCV genotypes, Genotype 1 is considered as the most common with an estimate of 49.1%, followed by genotype 3, 4 and 2 with a prevalence rate of 17.9%, 16.8% and 11.0% respectively. The distribution of G1, G2, G3, G4, G5, G6 and mixed genotypes in Asia are iden-

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tified as 46.6%, 18.6%, 22.4%, 1.0%, 0.1%, 7.0% and 4.3% respectively.⁷ In India, HCV prevalence has been estimated at 1-1.9% and as per the study in West Bengal, an increasing drift was found from children aged below 10 years (0.31%) to adults aged 60 years (1.85%); however, there is no significant difference observed between males and females.⁵ Various efforts such as, active screening of high-risk groups for HCV infection, provision of safe blood and blood products, avoiding unsafe injection practices, adequate awareness and education and effective vaccination programs have been implemented in order to prevent HCV in India, which eventually reduced the overall prevalence of HCV in India. Besides, the introduction of new direct-acting antiviral agents such as Sofosbuvir (in March 2015) followed by Ledipasvir and Daclatasvir (in December 2015) into the Indian market has strengthened the effective management of chronic HCV.⁸ According to a study conducted by Mahajan *et al.* has inferred that the HCV infection is mostly observed in the middle-aged rural males and the most observed risk factors were dental treatment, use of reused syringes and needles.⁷

HCV Genome

HCV is a single-stranded RNA virus, which is 9600 nucleotides in length that encodes for 3000 amino acids.⁹ All the seven genotypes exhibit their variability of about 30% at their nucleotide level. The single open reading frame forms a composition of the HCV genome, which encodes for ten proteins. These ten proteins consist of three structural proteins and seven non-structural proteins.¹⁰ Genotypes 1-4 and 6 have further multiple subtypes of genomes based on their genetic variability, while genotype 5 has only one subtype.¹¹ In the year 2006, genotype 7a was recognized for the very first time in the population of the democratic republic of Congo, further its subtype was identified and was named as GT7b.¹² Infection with Genotype 1 is the most all over the world, with the prevalence of 46% in the regions of Australia, Europe and North America. Genotype 3 has second the highest prevalence, i.e., 30%, after genotype 1 with predominance in the South Asian region, especially in India. It is observed that 23% of the HCV infections are due to genotypes 2, 4 and 6, while genotypes 7 and five together account for <1% of the cases.¹³ Among all RNA viruses, HCV virus is believed to have a higher mutation rate, i.e., 2.5×10^{-5} mutations per nucleotide per genome.⁸ Borgia MS *et al.* have reported the identification of newer genotype, i.e., GT 8 in Canada (in people those who are migrated from Punjab, India).⁵ A study conducted in Uttar Pradesh by Prakash *et al.* reported that the prevalent genotypes and subtypes

of HCV was found to be 25%, 2.9%, 0.25%, 68.07%, 2.2%, 0.49%, 0.74% and 0.24% for the genotypes 1a, GT1b, GT1c, GT3a, GT3b, GT3g, GT3i and GT4a, respectively.¹⁴ Whereas HCV genotypes GT2, GT5 and GT6 were not detected in that population and GT3a and GT1b were the commonest.

HCV Genotype-8

The novel HCV genotype eight was discovered by Borgia MS and team in four patients, who were taking part in POLARIS study in Canada, who were the immigrants of Punjab, India.⁵ Genotype 8 is distinct from other genotypes, with a variation of more than 30% in genotypic sequence and the NS-5B gene regions have an absence of 90 amino acids. Patients infected with GT 8 were previously misdiagnosed with GT 5 infection, which was performed by using a LiPA or Abbott Real Time PCR commercial assay.⁴ Borgia *et al.* also mentioned that among all four patients sustained viral response was achieved in all the four patient, two patients were on sofosbuvir/velpatavir/voxilaprevir regimen for eight months while other two were on sofosbuvir/ledipasvir for months and sofosbuvir/daltatavir for 12 months respectively. Regions like NS3, NS5A and NS5B were investigated for amino acid positions responsible for resistance and no amino acid responsible for resistance was present NS5 B region. NS5A, RASs, Q30S and Y93S region amino acid shows resistance to ledipasvir.⁵

CONCLUSION

In order to develop better sophisticated drug regimen for the HCV treatment, a keen knowledge regarding the novel genotypes is required at the population level, not just limiting it to the healthcare policy decision makers. There exists an epidemiological gap, as all the four patients reside in Canada; however, they were originally from India. Thus, further robust research is needed in the resource-limited countries like India where the HCV is considered as an epidemic, to discover additional patients with GT 8.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

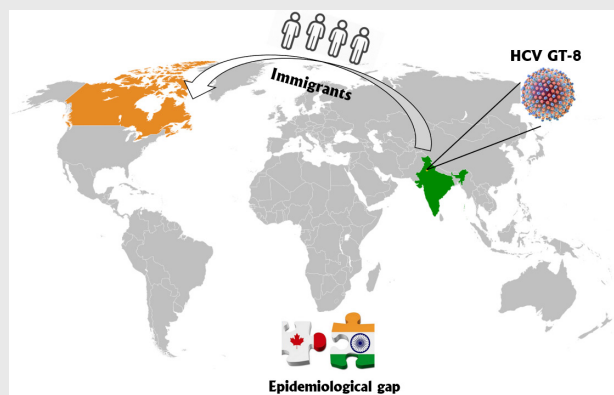
HCV: Hepatitis C Virus; **GT:** Genotype; **RNA:** Ribonucleic acid; **HCC:** Hepato-Cellular Carcinoma; **IV:**

Intravenous; **NS**: Non-structural protein; **PCR**: Polymerase chain reaction.

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PICTORIAL ABSTRACT



SUMMARY

- Hepatitis C Virus is a single-stranded RNA virus that belongs to the genus Hepacivirus of family Flaviviridae which is highly diverse and pervasive disease around the globe, with a prevalence ranging from 1.5 to 2.3%.
- HCV was categorized into seven genotypes with 67 subtypes until the discovery of genotype 8 that added 17 subtypes to the family of HCV, which make up the total to 8 genotypes with 84 subtypes.
- Getting familiarized and making aware of the HCV genotypes and subtypes is necessarily essential in establishing the optimal treatment regimen.
- There exists an epidemiological gap, as all the four patients reside in Canada; however, they were originally from India.
- Thus, further robust research is needed in the resource-limited countries like India, where the HCV is considered as an epidemic, to discover additional patients with GT 8.

About Authors



Dr. Sai Krishna Gudi, is a Ph.D. research scholar at the College of Pharmacy, University of Manitoba, Canada. Of now, he has authored around 30 papers that were published in both national and international journals. So far, he has attended various seminars, conferences and workshops, and presented numerous poster and oral presentations in the field of Pharmacy around the world. Besides, he is a member of numerous national and international societies. Throughout his journey in the profession of Pharmacy, he has received various scholarships and awards for his academic and research excellence. His research interest includes knowledge translation through Evidence-Based Practice, Optimizing Rational Drug-use, Pharmacoepidemiology, Pharmacy Education, Pharmacist Interventions, Patient-oriented Outcomes, and various aspects of Pharmacy Practice and Clinical Pharmacy.



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