

REVIEW ARTICLE:

Epidemiological Patterns of Genotype Distribution among Hepatitis C Patients in India: A Narrative Review

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ABSTRACT

Different genotypes of Hepatitis C have different epidemiological and clinical features, showing varying prognostic implications. This review captures the genotype distribution among Hepatitis C patients in India. The most predominant Hepatitis C virus genotype in India is GT3, followed by GT1, which is also significantly prevalent. GT4 and GT6 are increasingly prevalent in southern and north-eastern parts of India, respectively. Other rare genotypes such as GT2, GT5, and GT8 have also been reported across various parts of India. Among the primary modes of HCV transmission, intravenous drug use is more common in the younger population, while haemodialysis-related transmission is more prevalent among elderly males. HCV GT3 and GT1 appear to have a strong association with the patients being infected through intravenous drug abuse and haemodialysis, respectively.

Keywords: Hepatitis C, genotype, Intravenous drug abuse, haemodialysis, epidemiology, India

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Introduction

Hepatitis C virus (HCV) is a major global public health challenge, with considerable variation in prevalence and genetics that further complicates epidemiological surveillance, diagnosis, and treatment.

There is significant global variability in Hepatitis C prevalence, with low rates (<2.5%) in regions like North America, Europe, and Australia; moderate levels (2.5–10%) Middle East and South America; and high rates (>10%) in some African nations¹. GT1 is the most common HCV strain globally, accounting for 46.2% of infections, with subtypes 1a and 1b making up 90% of these cases. GT 3 follows at 30.1%, mostly in southern Asia and Scandinavia; while GT2, 4, and 6 make up 22.8% of infections worldwide. GT5 is rare (<1%), found mainly in South Africa, and GT7 was recently identified in a Canadian Congolese immigrant¹.

In 2019, analysis of HCV epidemiology synthesis Project database was conducted to study the epidemiology of HCV genotypes in Middle East and North Africa (MENA). The study found that GT1, which was common across the MENA region, was particularly more prevalent in high-risk clinical populations, such as haemodialysis. In contrast, GT3 was more prevalent in Afghanistan, Pakistan, and Iran, where it is associated with injection drug abuse. GT4 was widespread in Egypt and GT2 was more prevalent in high-risk clinical groups and those who inject drugs while its geographic variation remained unexplained².

It would be interesting to know the clinical parameters prior and after directly-acting antiviral therapy. SGOT ($p=0.053$) and creatinine ($p=0.050$) parameters exhibited a significant mean difference when compared between 1a and 1b intra-groups. But when 1b and 3 or 4 comparisons were made, SGOT and creatinine were found to be almost significant ($p=0.059$ and $p=0.061$, respectively); although, no parameter was statistically significant in this comparison as well³.

Hepatitis C genetic heterogeneity at intra-host and inter-host levels has significant impact on therapeutic management. This genetic diversity influences viral persistence, disease prognosis and transmission dynamics. Understanding this variability helps in the development of effective antiviral vaccines, treatment strategies and planning disease control measures and initiatives⁴.

There are reports to describe the global and regional distribution of HCV genotypes. A detailed report on the distribution of these genotypes for India is still lacking. Given India's vast social, and economic diversity, understanding the distribution of HCV genotypes is particularly important for optimizing treatment strategies and planning local and national administrative initiatives.

Data Sources

A comprehensive literature search was done in PubMed and EMBASE, using the following search terms: “[hepatitis c or HCV or hepatitis c virus] and [genotype or genotypes] and [India]”. All the observational studies were included in the review published after 2020. However, to address gaps in the synthesis, hand-searched articles were incorporated as needed. To strengthen this work and assess trends comprehensively, additional references, including those published prior to 2020, were also incorporated into the analysis.

Prevalence of Hepatitis C in India

The results of the systematic review by Chandra et al. (2024)⁵, involving 20 studies and 117661 participants, determined the prevalence of Hepatitis C in India to be 3.23%. As reported in this review, the HCV positivity rate of 0.33% by Tahashildar et al. (2023)⁶ at a tertiary care centre in South India.

Risk factors and socio-demographic features associated with HCV prevalence

According to Das et al. (2024)⁷, males had significantly higher odds of Hepatitis C infection compared to females (OR=2.78, 95% CI: 1.20–6.42, $p=0.013$). Similarly, individuals from rural areas also showed higher odds compared to urban residents (OR = 2.41, 95% CI: 1.29–4.48, $p=0.040$). Moreover, education ($P=0.002$), occupation ($p<0.00001$), marital status ($p=0.001$) and risk factors ($p<0.00001$) were also found to be significantly associated with HCV seropositivity⁶. Chakraborty et al. (2023)⁸ have shown that in north-eastern India among Hepatitis C patients, people who inject drugs (PWID) being the most common mode of transmission, majority of them were unmarried (84.4%), student (52.2%) and in the age group 21-30 years (57.8%)⁸.

Appalaraju et al. (2023)⁹ reported that the mean age of Hepatitis C patients at a tertiary care hospital in southern India was 56.47 ± 13.14 years and the majority of them were male (60.39%). Similar results were also reported by Tahashildar et al. (2023)⁶, highlighting a predominance of HCV seropositivity among males and individuals aged 41–70 years at a tertiary care hospital in south India⁶. Thoke et al. (2024) also reported matching findings, with a predominance of Hepatitis C cases among individuals aged 51–70 years in a zonal hospital in Meerut¹⁰. These results indicate a high prevalence of HCV seropositivity among elderly patients in hospitals, particularly among males.

In contrast, Das et al. (2024)⁷ reported that in Assam the majority of the HCV seropositive people who inject drugs were under 40 years of age³. Similarly, Kumar et al. (2023) like wise reported that the HCV seropositive cases in Bihar at an opioid-substitution therapy centre were predominantly in the age group of 18-40 years¹¹. These results infer that the Hepatitis C positivity in younger patients is mainly due to injecting drugs as the mode of transmission.

In the systematic review by Chandra et al. (2024), the highest prevalence was seen in blood transfusion group (38.55%), followed by general hospital (24.72%), risk behaviour groups (23.34%), and community (13.37%). Risk behaviour groups include men sex with men (MSM), blood donors, injection drugs user (IDU)⁵.

In another systematic review by Shalimar et al. (2022)¹², which studied risk factors for hepatitis C virus among low-risk groups in India, hospital visitors, community population, pregnant women, blood donors, individuals with diabetes mellitus, army recruits, and slum dwellers. This review confirmed blood transfusion, dental and obstetric procedures, surgical procedures, unsafe or multiple injections, body piercing, tattooing, and contaminated shaving as the risk factors. The most prevalent risk factors of them were unsafe or multiple injections (54.3%), followed by obstetric procedures (30.6%) and body piercings (25.4%)¹².

Prevalence of Hepatitis C in high-risk groups

Haemodialysis: The findings of Rani et al. (2023) and Khullar et al. (2024) were consistent in reporting a high HCV positivity rate of 35-40% among patients undergoing haemodialysis^{13,14}.

Rani et al. (2023) revealed a male predominance, with 80% of HCV-positive patients being men, which could be linked to a higher prevalence of chronic kidney disease. It also found that the 41–60 years aged group had a high HCV positivity rate (48%)¹³. Similarly, Reddy et al. (2023) also reported that 51.85% patients were from the age group of 41-60 years. It can be inferred that HCV positivity being linked to higher prevalence of chronic kidney disease in older men¹⁵.

People who inject drugs: Kumar et al. (2023), at an opioid-substitution therapy, reported the HCV seropositivity rate as 28% (95% CI: 22.7%-33.8%). Moreover, the highest positive rate of 47.1% was found in the patients who were injecting drugs for more than 10 years (6.3%)¹¹. Shukla et al. (2023)¹⁶ in their systematic review involving 50 studies, reported considerable heterogeneity in HCV prevalence among PWID across India. The prevalence of HCV among injecting drug users was reported to be as high as 97.5% in Manipur (1996) and 73% in Uttar Pradesh (2021)¹⁶. Further, due to shared routes of transmission, there is high prevalence of HBV and HIV among hepatitis C patients. Das et al. (2024) reported the HIV and HBV coinfection rates as 17.8% and 3.42%, respectively⁷. Solomon et al. (2019) reported a high prevalence of HCV seropositivity among HIV-positive PWID¹⁷.

HIV patients: Chhina et al. (2020) reported a Hepatitis C co-infection prevalence of 10.6% among 104 HIV patients in north India. Additionally, the mode of transmission was predominantly unprotected sexual behaviour (76%), followed by the use of contaminated needles (13.5%), and intravenous drug use (10.5%)¹⁸.

Another systematic review by Goel et al. (2018)¹⁹ has confirmed the pooled prevalence of Hepatitis C in HIV patients and in multi-transfused groups as 3.51% (2.43%-4.76%) and 24.06% (20.00%-28.36%), respectively. In contrast, the pooled prevalence of Hepatitis C in PWID, on maintaining haemodialysis are 44.71% (37.50%-52.03%) and 24.06% (20.00%-28.36%), respectively¹⁹.

The percentage-wise genotype distribution of Hepatitis C patients has been extracted in **Table 1**

Genotype distribution of Hepatitis C across India

North-eastern India: Das et al. (2024), Barman et al. (2022) and Chakraborty et al. (2024) have reported that the genotype most prevalent in north-eastern India was GT3 (50%-96%) followed by GT1 (3%-25%)^{7,20,8} (Table-1). Moreover, the most significant mode of transmission among them was injecting drugs of abuse. Das et al. (2024) also reported one case each of GT-6xa and GT-8. GT-6 is increasingly being identified mostly in the north-eastern states, sharing a border internationally with Myanmar, one of the ‘Golden Triangle’ countries, dominated by GT6.⁷

The findings were consistent with those of Solomon et al. (2019), who reported GT3 as the predominant genotype among HIV-infected PWID in north-eastern India¹⁷. In contrast, a study by Medhi et al. (2014) in the tribal population from Assam with 34.6% people who inject drugs, reported GT4 as the predominant genotype followed by GT3, GT1 and GT2²¹.

Southern India: Appalaraju et al. (2023) have reported that GT4 (35.71%) was the most prevalent variant in southern India, followed by GT3 (17.53%) and GT1 (12.99%). The increasing percentage of GT4 in South India could be attributed to migration of population from parts of world dominated by GT4.⁹

Although, the results of Tahashildar et al. (2023) were contradictory where the major genotype prevalent was GT1 (54.76%), followed by GT3 (38.09%) and GT4 (4.76%) ⁶ (Table 1).

Table - 1: Genotype distribution among Hepatitis C patients with detectable HCV RNA

Author Year City/ State (Geography)	Size (No); Genotyping method	3	1	4	3&4	4&5	1 &3	6	8	Untypable sequences
		No. (%)	No. (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No (%)	No. (%)
Das, 2024 ⁽⁷⁾ Assam (North-East)	292;RT-PCR	280 (95.89)	10 (3.42)	--	--	--	--	1 (0.34)	1 (0.34)	--
Barman, 2022 ⁽²⁰⁾ Shillong (North-East)	130;Nested RT-PCR	77 (59.23)	34 (26.15)	--	--	--	--	19 (14.62)	--	--
Chakraborty, 2024 ⁽⁸⁾ Tripura (North-East)	90;RT-PCR	47 (52.0)	17 (18.9)	--	19 (24.7)	--	--	--	--	--
Appalaraju , 2023 ⁽⁹⁾ Tripura, South	154; Multiplex PCR	27 (17.53)	20 (12.99)	55 (35.7)	--	1 (0.65)	--	--	--	45 (29.92)
Tahashildar, 2023 ⁽⁶⁾ Tripura, South	42; CR-Fluore- scence	16 (38.09)	23 (54.76)	2 (4.76)	--	--	--	--	--	1 (2.38)
Shahanas, 2024 ⁽³⁾ Uttar Pradesh (North)	50; Kit-based assays	33 (66.0)	16 (32.0)	1 (2)	--	--	--	--	--	--
Thoke 2024 ⁽¹⁰⁾ Meerut (North)	59; Linear array HCV genotyping test	43 (72.88)	15 (25.42)	1 (1.69)	--	--	--	--	--	--
Gandhia, 2021 ⁽²⁵⁾ Surat (West)	23; Sanger technique	15 (65.0)	6 (26.0)	2 (9.0)	--	--	--	--	--	--
aYabaji 2018 ⁽²⁶⁾ Mumbai (Central)	120; RT-PCR	70 (58.3)	43 (35.9)	2 (1.7)	--	--	2 (1.7)	--	--	3 (2.5)
CR fluorescence: Congo Red fluorescence; RT-PCR: reverse transcription polymerase chain reaction Studies published 2020 onwards included in the table ^a study included is published before 2020, to provide a complete geographic overview of India Order irrespective of publication year to understand the variation in genotype distribution with respect to geography of India -- indicates no (0) cases of that particular genotype										

In contrast to both studies, the study by Rooby et al. (2014) found that GT3 was dominant (63.85%), followed by GT1 (25.72%) and GT4 (7.5%)²². Also, study by Christdas et al. (2019) reported GT3 as the dominant genotype, followed by GT1, GT4 and GT6.²³ These studies reveal a temporal shift in HCV genotype distribution in South India, reflecting dynamic changes over time.

Traditionally, GT4 of the Hepatitis C has been predominantly associated with the Middle East and Africa owing to its geographical isolation, which is considered resistant to treatment^{1,2}. However, recent trends indicate a rising prevalence of GT4 in South India. Our findings further reveal a significant presence of both GT1 and GT4 in South India, alongside the prominent GT3. The varying genotype distribution in south India could be attributable to varying distribution of risk factors among them.

Northern India: The Shahanas et al. (2024) and Thoke et al. (2024) consistently found that the GT3 (66-73%) is the most prevalent genotype in north India followed by GT1 (25-32%)^{3,10} (Table 1).The results of Thoke et al. (2024) and Shahanas et al. (2024) were in concordance with the study by Shah et al. (2016) among 607 hepatitis C patients at Kashmir, the most dominant genotype was GT3 (90.8%), followed by GT1 (8.1%), GT2 (0.3%) and GT4 (0.8%)²⁴.

Central and Western India: Gandhia et al. (2021) studied the genotype distribution in Surat (western India) among 23 detectable HCV RNA. It reported GT3 as the predominant genotype followed by GT1 and GT4,²⁵ (Table 1).

There was a lack of recently published studies for the genotype distribution among hepatitis C among patients from central and western India. However, some studies published in the last decade could be considered and general trends for Hepatitis C distribution could be extrapolated to these areas. Yabaji et al. (2018) studied the genotype distribution among 120 chronic hepatitis C patients in Mumbai. The predominant genotype was GT3 (58.3%), followed by GT1 (35.9%), GT1&3 (1.7%) and GT4 (1.7%)²⁶.

The results of Patil et al. (2018) in Maharashtra were consistent with these findings, GT3 being the most prevalent genotype followed by GT1⁷.

Table-2: Distribution of risk factors among Hepatitis C patients										
Author Year City/ State (Geography)	Size (No)	IV drug use	Tattooing piercing	Blood transf usion	Haemo- dialysis	Multiple sex	H/O surgery	Haemo- philiacs	Contact of known positive	Not Identified
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Das, 2024 ⁽⁷⁾ Assam (North- East)	292	74.31	33.22	10.27	9.25	--	--	--	--	--
Chakraborty, 2024 ⁽⁸⁾ Tripura (North- East)	90	88.90	--	4.4	6.66	--	--	--	1.37	--
Barman, 2022 ⁽²⁰⁾ Shillong (North-East)	130	77.69	2.31	2.31	6.15	3.84	--	--	--	7.69
Yabaji, 2018 ⁽²⁶⁾ Mumbai (Central)	--	0.83	--	51.67	21.7	--	9.17	3.33	--	--

Genotype distribution and mode of transmission of Hepatitis C

IV drug abuse: The Das et al. (2024), Barman et al. (2022) and Chakraborty et al. (2024) were concordant in reporting GT1 as the predominant genotype among Hepatitis C patients at a hospital or clinic in north-eastern India. The most significant mode of transmission among them was intravenous drug abuse (75-90%) (Table-2). Other risk factors include tattooing/ piercing, blood transfusion, haemodialysis and multiple sex ^{7, 20, 8}. Thus, IV drug abuse appears to be correlated to the predominant genotype as GT3 among Hepatitis C patients in north-eastern states. And, it can be conveniently concluded that the most prevalent genotype among the Hepatitis-C patients with intravenous drug abuse as the mode of transmission is GT3. Moreover, the findings of Solomon et al. (2019) along with the above findings in identifying GT3 as the most significant genotype among HIV-positive PWID¹⁷. Injecting drug use is recognized as a significant risk factor that contributes to both the local and broader transmission of Hepatitis C. Thus, controlling injecting drug abuse requires a collaborative effort from both local and national governments.

Table-3: Genotype distribution in patients with Hepatitis C maintaining haemodialysis

Author Year City/ State (Geography)	Size (No)	Detection Method	Preval- ence (%)	Detectable HCV RNA (No.)	Genotyping method	1 (No & %)	3 (No & %)	Untypable Sequences (No & %)
Suresh, 2025 ⁽²⁸⁾ Chennai (South)	86	CLIA	12.8	6	Versant HCV Genotype 2.0 Assay	6 (100)	--	--
Reddy, 2024 ⁽¹⁵⁾ Telangana (South)	27	ELISA	9.7	12	RT-PCR	10 (83.33)	2 (16.67)	--
Rani, 2023 ⁽¹³⁾ (South)	60	--	41.60	25	RT-PCR	24 (96)	--	1 (4)
Khullar, 2024 ⁽¹⁴⁾ Rajasthan (West)	109	--	35.78	24	RT-PCR and Line-probe assay	21 (87.5)	1 (4.17)	2 (8.33)
Roy, 2019 ⁽²⁹⁾ Pune (West)	250	ELISA	18.8	203	Big Dye Terminator cycle sequencing ready reaction kit	198 (97.3)	5 (2.7)	--
CLIA: Chemiluminescence immunoassay; ELISA: enzyme-linked immunosorbent Assay; RT-PCR: reverse transcription polymerase chain reaction								

Haemodialysis: Similarly, Suresh et al. (2025), Reddy et al. (2024), Rani et al. (2023) and Khullar et al. (2024) concurrently found that the majority of patients on maintaining haemodialysis with detectable HCV RNA were infected with GT1 (83-96%) (Table 3). These studies also reported the presence of GT3 in the HCV patients (Table 4) ^{28,15,13,14}. Therefore, GT1 appears to have a strong and consistent association with transmission through haemodialysis. The results were consistent with those of Roy et al. (2019), who reported GT1 as the predominant genotype among 204 patients on haemodialysis with detectable HCV RNA²⁹.

A general comment on genotype distribution among HCV patients on maintaining haemodialysis cannot be made, as no relevant studies from northern or eastern regions were included. Although, existing evidence suggests that GT1 is highly prevalent in southern India, the studies included in this review indicate an even greater predominance of GT1 among HCV patients undergoing maintenance haemodialysis. Conversely, patients infected with HCV GT1 could be more susceptible to developing end-stage renal disease, which accounts for the high prevalence of GT1 among haemodialysis patients.

Blood Transfusion: Dutta et al. (2023), in their prospective study in West Bengal (eastern India), showed that the HCV RNA was found in 65.21% of the 917 multi-transfused HCV sero-reactive β -thalassemia patients³⁰. The most dominant genotype was GT3a in 468 samples (78.26%), followed by GT1b in 72 cases (12.04%) and GT3b in 52 cases (8.70%). The other insignificant samples were genotypes 3g, 3i and 1a³⁰. This reflects the general genotype distribution of Hepatitis C in India. However, no other recent studies studying genotype distribution among Indian HCV patients, particularly undergoing blood transfusion were identified.

HIV and HCV co-infection: The genotype distribution among the special population of HIV co-infection is worth studying. Gupta et al. (2022) reported that among a total of 2,052 patients infected with HCV, GT6 was found in 2.5% of cases³¹. The highest percentage (81.1%) of GT6 among HCV individuals was observed in those co-infected with HIV. Nine different GT6 subtypes were identified—namely 6a, 6b, 6f, 6i, 6n, 6u, 6v, 6w, and 6xa. Although, 6xa was the most prevalent (41.5%), followed by 6n (39.6%)³¹.

Untypable and mixed genotypes

Untypable sequences: The presence of unclassifiable HCV genotypes in certain samples suggests inherent shortcomings in traditional genotyping methods. This observation emphasizes the growing significance of advanced molecular tools like whole genome, next-generation sequencing (NGS), which are better equipped to resolve uncertainties in genotype determination. The deployment of advanced techniques, such as next-generation sequencing and Sanger sequencing, is essential in cases of retreatment and drug resistance.

Mixed genotypes: Chakrobarty et al. (2024) identified mixed genotype (3 & 4) in 24.7% of the Hepatitis C patients in north-eastern India, as determined by RT-PCR⁸. Peer et al. (2024), in their prospective study in Uttar Pradesh, 70% of the samples were infected with multiple genotypes, as identified by RT-PCR (Reverse transcription polymerase chain reaction) followed by agarose gel electrophoresis³². Patients infected with multiple HCV genotypes exhibited higher rates of clinical complications, compared to those with single-genotype infections—predominantly fatty liver (7 vs 1), followed by hepatomegaly (4 vs 0), splenomegaly (2 vs 1), abdominal pain (2 vs 1), and liver cirrhosis (1 vs 1)³².

Author Perspective: It is recommended that clinics/ health-care facilities handling HCV in India should explore the opportunity of genotyping. The genotyping shall assist in better treatment guidelines. Additionally, there is a significant gap in literature from India focusing on the genotype distribution of Hepatitis C, required to synthesize higher levels of evidence.

Conclusion

Overall, GT3 is the predominant Hepatitis C virus genotype in India, followed by GT1, which is also significantly prevalent. GT4 and GT6 are increasingly prevalent in southern and north-eastern parts of India, respectively. Other rare genotypes such as GT2, GT5, and GT8 have also been reported in India. Intravenous drug use is the most significant mode of Hepatitis C transmission overall, and is particularly prominent among the younger population, showing a strong association with GT3

infections. In contrast, haemodialysis is another significant mode of transmission associated with a high prevalence of Hepatitis C GT1 infection, in addition to GT3 infection.

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