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Original Research Article

Clinical Spectrum and Genotypic Characterisation of Hepatitis-C Infection: A Cross-Sectional Study in a Teaching Hospital in Tripura

Abhishek Chakraborty[1]*, Parimal Sarkar[2], Pradip Bhaumik[3]

[1]Senior Resident, Department of Medicine, Agartala Government Medical College & GBP Hospital
[2]Associate Professor, Agartala Government Medical College & GBP Hospital
[3]Professor, Department of Medicine, Agartala Government Medical College & GBP Hospital

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Corresponding Author: Dr. Abhishek Chakraborty
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Abstract:

Introduction: Hepatitis C virus (HCV) is a major health challenge affecting around 200 million people worldwide, causing liver fibrosis, cirrhosis, and cancer. Despite no vaccine, advancements in treatment have led to cures. In India, HCV causes up to 21% acute viral hepatitis and 14-26% chronic liver disease. HCV is classified into six genotypes and 67 subgenotypes, with India having genotype 3. Understanding viral persistence and transmission modes is crucial for HCV prevention and designing therapeutic strategies. Screening and quantification of HCV are crucial for diagnosis and treatment, and early identification can lead to effective antiviral therapies. HCV genotype also influences treatment, as RNA viruses evolve and respond differently across regions. Understanding genotype distribution is crucial for therapy efficacy and estimating disease burden in Tripura. HCV is a small, positive polarity, enveloped virus from the Hepacivirus genus, with a high mutation rate generating genetic diversity within hosts.

Aims & Objective: The study aims to analyze Hepatitis-C genotypic and clinical characteristics in GBPH and AGMC patients, examine their range, and estimate viral load to assess Sustained Virological Response.

Methods: This observational study, conducted at the Dept. Of Medicine, AGMC & GBPH, aimed to analyze the impact of viral hepatitis on patients attending both the Obstetrics and Gynecology Outpatient Department (OPD) and the Inpatient Department (IPD). The study was conducted over two years, with a sample size of all patients meeting inclusion and exclusion criteria. The study used a predesigned proforma to collect demographic data, medical history, and clinical features. The study excluded cases with HCV already identified and receiving treatment.

Results: The study analyzed data from 90 Hepatitis-C patients at Agartala Government Medical College and GBP Hospital, West Tripura, focusing on their history, examination, and laboratory tests.

Discussion: The study on Hepatitis C (HCV) infection in Tripura, India, from January 2021 to June 2022, found that it is more prevalent among younger individuals due to drug use. The majority of patients were students under 30, with 23.3% being drivers. Intravenous drug use (IDUs) was the most common mode of transmission, followed by regular hemodialysis and multiple blood transfusions. Risk factors include unsafe sexual practices, IDU, injection practices, tattooing, and acupuncture. The study also found a significant reduction in HCV RNA after 12 weeks of antiviral therapy, achieving a 96% SVR.

Conclusion: A study revealed that Chronic Hepatitis-C is primarily affecting the young generation, with mixed genotypic infections and a prevalence of 31%. The effectiveness of current DAAs and a national initiative are still being evaluated.

Keywords: HCV, Hepacivirus genus, genotypic characterization, IDU.

Introduction

Prometheus' liver was tortured in Greek mythology, and liver diseases have evolved significantly. Hepatitis C virus (HCV) is a major health challenge, affecting around 200 million people and causing liver fibrosis, cirrhosis, and cancer. Despite no vaccine, advancements in treatment have led to cures. In 2020, Nobel Prize Medicine was awarded to Harvey J. Alter, Michael Houghton, and Charles M. Rice. [1,2] In India, HCV causes up to 21% acute viral hepatitis and 14-26% chronic liver disease, with 1% anti-HCV Ab prevalence, with 80% having detectable HCV RNA.[3,4] HCV, an RNA virus, is classified into six genotypes and 67 subgenotypes based on genomic variability. India has genotype 3, while North America, Europe, Middle East, Africa, South Africa, and South-East

Asia have genotypes 1, 2, 3, 4, and 5, respectively. [5] India's HCV genotype 3 is prevalent in northern, eastern, and western parts, followed by genotype 1 in southern India, accounting for approximately 63.85% of the total HCV genotypes.[6]

Despite the widespread prevalence of genotypes 3 and 1, there is an increased prevalence of genotypes 4 and 6 in certain regions of India, particularly in south Indian patients, north eastern parts of India, and Myanmar. [7]

Understanding viral persistence and transmission modes is crucial for HCV prevention, and genotype knowledge and viral load assessment are essential for designing therapeutic strategies and predicting treatment outcomes. Screening and quantification of HCV are crucial for diagnosis and treatment of related diseases. Early identification can lead to effective antiviral therapies. However, chronic infection can be challenging and ineffective. HCV genotype also influences treatment, as RNA viruses evolve and respond differently across regions. Genotype and sub-genotype determination aids in studying population-migration patterns in the NE region, particularly in Tripura, where most population groups have migrated from outside India. This study provides insight into heterogenous migration patterns and therapy response through viral molecular analysis.

AGMC's Liver Clinic treats Hep-C patients, providing a comprehensive view of disease patterns. Understanding genotype distribution is crucial for therapy efficacy. The study evaluates HCV demographics, viremia rates, and genotype distribution to estimate disease burden in Tripura and understand socioeconomic factors affecting prevalence.

Hepatitis C virus (HCV) affects 180 million people globally, with annual new infections increasing by three million. HCV is a leading cause of chronic liver disease, with 20% developing cirrhosis and 10% developing cancer. [8,9] HCV is a small, positive polarity, enveloped virus from the Hepacivirus genus. Its RNA genome consists of a polyprotein with a 5'- and 3'-untranslated regions, including an internal ribosomal entry site for viral replication.

The polyprotein is processed into three structural proteins and seven nonstructural proteins. The HCV core is a conserved protein, while E1 and E2 are glycosylated proteins involved in cell entry. NS2 is a transmembrane protein required for viral replication, while NS3 is the HCV protease and NTPase/helicase. [10-14]

HCV virions bind to host cellular receptors via E2, with multiple receptors identified. Once bound, HCV particles are internalized through pH-dependent and clathrin-mediated endocytosis. Upon entry, the viral genome is released, translated, and membranous webs form for replication. Progeny virions are assembled and released by the constitutive secretory pathway. [15, 16] The high mutation rate of HCV generates genetic diversity within hosts, allowing rapid adaptation and persistence.

This molecular plasticity is crucial for virus transmission, disease progression, and therapy outcomes and understanding its mechanisms could aid in controlling HCV-related diseases.

Aim

To investigate the genotypic and clinical characteristics of Hepatitis-C in individuals receiving care at GBPH and AGMC.

Goals

1. To examine the genotypic and clinical range of Hepatitis-C in the study population.
2. To estimate the viral load in relation to genotypic pattern in order to evaluate the Sustained Virological Response (SVR) at 12 weeks of anti-HCV medication.

Methodology

Study Type: Observational study.

Study Design: Cross-sectional, Time-dimensional study.

Study Setting: This is a Hospital-based study and was conducted in Dept. Of Medicine, AGMC & GBPH

Study Duration: This study was completed within 2 years of duration [one and half year for data collection (January 2021 to June 2022) and 6 months for data management].

Study Population: All patients attending both OPD and IPD of AGMC and GBPH patients irrespective of their age & sex for treatment during the study period.

Sampling Technique: All the patients to be taken through Census sampling after fulfilling the inclusion and exclusion criteria

Sample Size: As it is a census sampling technique all the patients fulfilling the inclusion criteria was taken as sample size.

Study Tool: A predesigned proforma was used to collect relevant information, demographic data, medical history and clinical features for each patient using a standard questionnaire.

Investigations were done and the clinical details and the investigations reports was recorded and used for data analysis.

Inclusion Criteria:

1. Individuals who exhibit viral hepatitis symptoms.
2. Known cases of HIV-positive patients receiving hemodialysis and frequent blood transfusions, as well as CLD and HCC cases.
3. Patients who have risk factors such as long-term alcoholism, sex workers, injectable drug users, or homosexuals.
4. Medical Professionals.
5. HCV patients with positive ELISA results who are scheduled for prenatal checkups in the Obstetrics and Gynecology OPD.

Exclusion Criteria:

Cases with HCV already identified and receiving treatment.

Over the course of the study, when they visit the IPD and OPD (LIVER CLINIC), every case will be chosen one after the other. We will employ an interview schedule to collect all necessary data, including their blood reports. The following need to be looked into:

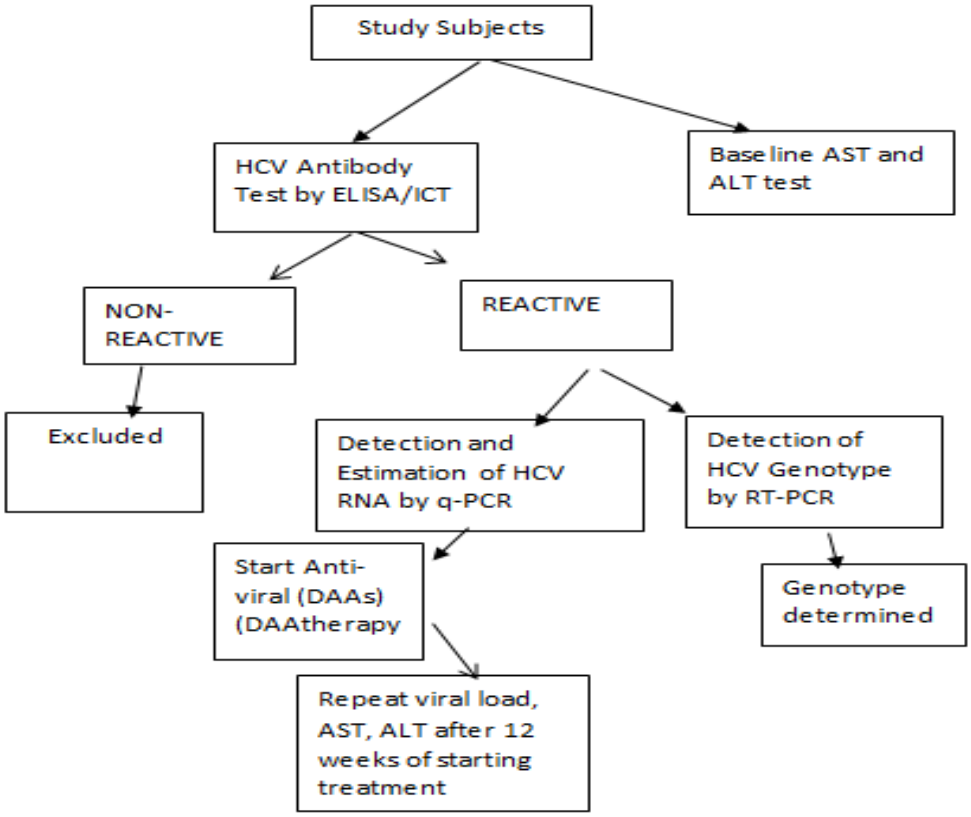

Chart 1:

Statistical Analysis

The study used Microsoft Excel and SPSS to analyze data, summarizing numerical and categorical variables as mean and standard deviation, and conducting two-sample t-tests to determine differences in mean between independent or unpaired samples.

The Z-test was utilized to examine the significant difference in proportions. Various t-tests are provided with explicit expressions, formulas for test statistics, and appropriate degrees of freedom for one-tailed and two-tailed tests. These statistics can be used for a null hypothesis or closely approximate a t-distribution.

A t value is determined, and a p-value is calculated using Student's t-distribution table. If the p-value falls below the statistical significance threshold, the null hypothesis is rejected for the alternative hypothesis.

P-value ≤ 0.05 was considered for statistically significant.

Result and Analysis

The study, conducted from January 2021 to June 2022, involved 90 cases from the Liver OPD and IPD of Agartala Government Medical College and GBP Hospital, West Tripura.

The study analyzed data from 90 Hepatitis-C patients who met the inclusion criteria, observing and deducting observations and deductions.

After taking informed consent, required history, examination and laboratory tests were performed as described in the case format.

Table 1: Distribution of Age in Group

Age in group	Frequency	Percent
≤21	28	31.1%
21-30	52	57.8%
>31	10	11.1%
Total	90	100.0%

The study included 28 patients aged ≤21 years, 52 patients aged 21-30 years, and 10 patients aged >31 years. The value of z is 6.5879. The value of p is < 0.00001. The result is significant at p < .05.

Table 2: Distribution of Sex

Sex	Frequency	Percent
Male	90	100.0%
Total	90	100.0%

The study involved 90 male patients, accounting for 10.0% of the total population.

Table 3: Distribution of Religion

Religion	Frequency	Percent
Buddhist	10	11.1%
Christian	10	11.1%
Hindu	66	73.3%
Muslim	4	4.4%
Total	90	100.0%

The study included a diverse group of patients, including Buddhists (11.1%), Christians (11.1%), Hindus (73.3%), and Muslims (4.4%). The statistical analysis yielded a significant result at a p-value of less than 0.05.

Table 4: Distribution of Occupation

Occupation marital	Frequency	Percent
Driver	21	23.3%
Jobless	15	16.7%
Shopkeeper	7	7.8%
Student	47	52.2%
Total	90	100.0%

The study surveyed 21 patients, with 23.3% being drivers, 16.7% being jobless, 7.8% being shopkeepers, and 52.2% being students. The statistical analysis indicates a significant result at a significance level of p <.05.

Table 5: Distribution of Marital Status

Marital Status	Frequency	Percent
Married	14	15.6%
Unmarried	76	84.4%
Total	90	100.0%

The study found that 15.6% of patients were married, while 84.4% were unmarried, indicating a significant difference at a p-value of less than 0.05.

Table 6: Distribution of PWID

PWID	Frequency	Percent
No	10	11.1%
Yes	80	88.9%
Total	90	100.0%

The study involved 80 patients, with 88.9% of them having PWID. The statistical analysis indicates a significant result at a significance level of p <.05.

Table 7: Distribution of Multiple Blood Transfusion

Multiple blood transfusion	Frequency	Percent
No	86	95.6%
Yes	4	4.4%
Total	90	100.0%

The study involved 4 patients (4.4%) who underwent multiple blood transfusions. The statistical analysis yielded a significant result at a p-value of less than 0.05.

Table 8: Distribution of Regular Hemodialysis

Regular Hemodialysis	Frequency	Percent
No	88	93.4%
Yes	6	6.66%
Total	90	100.0%

The study revealed that 6.66% of patients who were on regular hemodialysis had a hepatitis-c infection. The statistical analysis indicates a significant result at a p-value of less than 0.05.

Table 9: Distribution of Others

Others	Frequency	Percent
H/o surgery	00	0.00%
No	90	100%
Total	90	100.0%

The study found that all patients had no heart failure surgery. The statistical analysis indicates a significant result at a significance level of $p < 0.05$.

Table 10: Distribution of HCV Genotype

HCV Genotype	Frequency	Percent
1	17	18.9%
3+4	19	24.7%
3	47	52%
6	4	4.4%
Total	90	100.0%

The study found that 18.9% of patients had HCV genotype 1, 24.7% had genotype 3+4, 52% had genotype 3, and 4.4% had genotype 6. The statistical analysis indicates a significant result at a significance level of $p < 0.05$.

Table 11: Distribution of HCV Elisa

HCV Elisa	Frequency	Percent
Positive	90	100.0%
Total	90	100.0%

The study involved 90 patients (100.0%) who had HCV Elisa.

Table 12: Distribution of Liver Function At Baseline

Clinical Features	Frequency	Percent
Normal	80	88.9%
Raised AST, ALT	10	11.1%
Total	90	100.0%

The study found that 88.9% of patients had normal clinical features, while 11.1% had raised AST and ALT at baseline. The statistical analysis indicates a significant result at a significance level of $p < .05$.

Table 13: Distribution of Liver Function at 12 Weeks after Treatment

Clinical Features	Frequency	Percent
Normal	87	96.6%
Raised AST, ALT	3	3.3%
Total	90	100.0%

The study found that 97% of patients had normal clinical features, while 33% had raised AST and ALT levels after 12 weeks of treatment completion. The statistical analysis indicates a significant result at a significance level of $p < .05$.

Table 14: Distribution of Mean Age (Year)

	Number	Mean	SD	Minimum	Maximum	Median
Age	90	24.5889	6.9588	19.0000	43.0000	23.0000

The table indicates that the mean age of the patients was 24.5889 ± 6.9588.

Table 15: Distribution of Mean HCN RNA Load at Baseline (Iu/L)

	Number	Mean	SD	Minimum	Maximum	Median
HCN RNA Load at Baseline (IU/L)	90	1661712.3333	2502710.9603	35300.0000	8160000.0	351450.0

The table indicates that the mean HCN RNA Load at Baseline (IU/L) for patients was 1661712.3333 ± 2502710.9603.

Table 16: Distribution of Mean HCV RNA Load at 12 Weeks

	Number	Mean	SD	Minimum	Maximum	Median
HCV RNA Load at 12 weeks	90	2919.1111	8206.0430	34.0000	26000.0000	34.0000

The table indicates that the mean HCV RNA Load of patients at 12 weeks was 2919.1111 ± 8206.0430.

Discussion

This observational study focuses on the burden of Hepatitis C (HCV) infection in Tripura, India, from January 2021 to June 2022. The study reveals that HCV infection is more prevalent among younger individuals due to drug use. The study found that 52 patients were aged 21-30 and 90% were male. This is consistent with previous studies indicating a male predominance.[17]

The study reveals that 52% of patients are students under 30 years old, with 23.3% being drivers, indicating a high risk group for HCV epidemiology due to injectable drug use. The study reveals that intravenous drug use (IDUs) is the most common mode of transmission for Hepatitis-C (HCV), followed by regular hemo-dyalysis (6.66%) and multiple blood transfusions (4.4%). Risk factors include unsafe sexual practices, IDU, injection practices, tattooing, and acupuncture. [18,19] Drug abuse in northeastern states like Tripura is a major issue due to the 'Golden Triangle"s illicit drug production and trafficking. Injecting Drug Users (IDUs) in India are at high risk of contracting HCV infection due to unsafe practices. [20]

The study reveals a higher prevalence of genotype 3 (52%) in Tripura, with a higher prevalence in North East India. Mixed infection (genotype 3+4) is prevalent in 24.7% of study subjects. Previous studies have shown mixed genotypic infection in northern India, with a prevalence of 31% in genotype 3+4. [21] The study shows a significant reduction in HCV RNA after 12 weeks of antiviral therapy, particularly Sofosbuvir and Daclatasvir, in most Non-cirrhotic Chronic Hepatitis-C patients, achieving a 96% SVR, based on a 2017 Indian study. [22]

The study assessed ALT and AST at baseline and 12 weeks post-treatment, showing a significant reduction in abnormal values after 12 weeks of DAA therapy in Chronic Hepatitis-C patients. This suggests that AST, ALT, or AST/ALT ratio could be a useful early, easy, and low-cost method for liver pathology assessment. [23]

Summary

The study found that the majority of patients were aged 21-30, predominantly Hindu, students, drivers, and shopkeepers. Many were jobless, with a lower number of married patients. The majority had PWID, multiple blood transfusions, and regular hemodialysis. Most patients had HCV genotype 3 or mixed genotypic infection. After 12 weeks of anti-viral therapy, the mean HCV RNA level decreased to <34, indicating normalization.

Conclusion

A study at Agartala Government Medical College & GBP Hospital in Tripura, India, found that Chronic Hepatitis-C is primarily affecting the young generation, with increased intravenous drug use and proximity to countries like Bangladesh. The study also revealed mixed genotypic infections, with a prevalence of almost 31%.

The effectiveness of current Drug Administered Antivirals (DAAs) in reducing viral load and abnormal liver enzymes is still being evaluated. As no Hepatitis-C vaccine is available, a national initiative is needed to prevent the disease's transmission.

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