

ORIGINAL RESEARCH ARTICLE

DEMOGRAPHIC, CLINICAL AND VIROLOGICAL PROFILE OF PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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ABSTRACT

Background: Chronic Hepatitis C virus (HCV) is a major public health issue worldwide. Chronic HCV is an important cause of cirrhosis and hepatocellular carcinoma. Hepatitis C infection is not uncommon in Nepal. This research was meant to study the demographic, clinical presentation, and virological profile of patients with chronic hepatitis C attending a teaching hospital in Western Nepal.

Methods: A hospital-based, cross-sectional study was conducted over a year from January 2021 and December 2021 among 66 consecutive patients with hepatitis C infection. Demographic and clinical profile of the patients alongside their liver enzymes, viral load, and genotypes at the time of presentation were studied. Descriptive analysis was done using SPSS version 20.

Results: The mean age of subjects was 34±10.42 years with male predominance (M: F=2.3:1). The majority was from rural areas and belonged to low-middle socioeconomic status. Injecting drug use was the most common mode of infection. The majority of patients had no symptoms related to liver diseases. About one-fourth of the patients had cirrhosis of liver. High viral load (HCV RNA > 800,000 IU/ml) was detected in 42.4% patients. The mean HCV RNA was 1348,500 ±1052 IU/ml. Genotype 3a was the most common, followed by genotype 1a.

Conclusions: Hepatitis C virus infection was common in young patients (aged <40 years) especially among injecting drug users. Most of the patients had no symptoms related to liver diseases. Cirrhosis was observed in about one-fourth patients. Genotype 3a was the most common, followed by genotype 1a.

INTRODUCTION

Hepatitis C virus (HCV) infection is a major public health issue all around the world. About 71 million people or 1% of the world's population are infected with HCV.¹ An estimated 27% of cirrhosis and 25% of hepatocellular carcinoma (HCC) is attributed to HCV worldwide.² Hepatitis C virus infection accounts for approximately 15–20% of cases of acute hepatitis. After an acute infection, around 70–85% of HCV patients will develop chronic infection.³

Hepatitis C virus belongs to the Flaviviridae family, consists of positive-sense single-stranded RNA virus with six genotypes. Genotypes of HCV 1, 2, and 3 are distributed globally, while genotype 3 is dominant in South Asia.⁴ Genotypes 4, 5, and 6 are predominant in the Middle East and Central Africa, Southern Africa and Southeast Asia respectively.⁴

Chronic HCV infection (infection > 6 months) is marked with elevated liver enzyme, serum alanine aminotransferase (ALT). However, 25-30% of individuals with chronic HCV infections can still have persistently normal ALT levels.⁵ The treatment of

HCV infection has improved with the introduction of directly acting antiviral (DAAs) agents used according to genotypes and stages of disease.^{6,7}

Due to unavailability of vaccine, delay in the diagnosis and limited access to treatment, chronic HCV continues to be important cause of cirrhosis and hepatocellular carcinoma especially in developing countries. The prevalence of hepatitis C was 3.7% among patients attending an infectious disease hospital in Nepal.⁸ This research was meant to study the demographic, clinical presentation, and virological profile of patients with chronic hepatitis C attending department of Medicine at Manipal Teaching Hospital, a tertiary care center in Western Nepal.

METHODS

A hospital based, cross-sectional study was carried out among hepatitis C patients who attended the unit of Medical Gastroenterology, under the department of Medicine between January 2021 and December 2021 over a period of 12 months. The study was approved and verified by the Institutional

Review committee (MEMG/IRC/ 428/GA). Informed consent was obtained from patients or patient relatives.

The sample size was collected using the formula:

$$\text{Sample size: } Z^2 \times [p \times (1-p)] / e^2$$

Z: 1.96 (critical value of the normal distribution for 95% confidence interval)

p: prevalence, q=1-p

e: margin of error (0.05 i.e. 5%)

The prevalence of hepatitis C was 3.7% in a previously published hospital study from Nepal.⁸ The minimum sample size required with this prevalence and calculated as per the equation was 54.75. So, the minimal sample size was 55.

All consecutive patients aged 18 years and above who were sera positive for Hepatitis C for more than 6 months were enrolled for the study. Patients under medication or who had taken antiviral or interferon in the past, unavailability of viral load (HCV RNA) reports, and those who did not give consent were excluded from the study.

The evaluation included clinical history of the patients, particularly how it was diagnosed, and the possible modes of transmission of hepatitis C. Clinical examination included general and abdominal examination. Liver cirrhosis was diagnosed clinically with evidence of jaundice, ascites, stigmata of chronic liver disease and other features of decompensation. This was further supported by an assessment of liver parenchyma, its echogenicity, presence of portosystemic collaterals, and other findings of portal hypertension by ultrasonography and/or Computed tomography of the abdomen. Rapid diagnostic test kits (HCV TRI-DOT, J. Mitra & Co. Pvt. Ltd.) were used as screening tests for the detection of antibodies to hepatitis C virus in serum. Confirmation was done by enzyme-linked immunosorbent assay (Anti HCV-ELISA).

Liver function test was done along with screening for Hepatitis B and HIV as well. Ultrasonography of the abdomen was done in all subjects. All the included patients were positive for HCV RNA by Real-Time- Polymerase Chain Reaction (PCR). The virological profile included both viral load and HCV genotypes. HCV genotype and HCV viral load quantification facility was not available in our hospital. The blood sample was collected and sent to Decode Genomics and Research Center (a Government approved lab in Kathmandu Nepal) maintaining a cold chain where HCV RNA quantification and HCV genotyping was performed. HCV RNA quantification was done using RealStar[®] HCV RT-PCR Kit from Altona Diagnostic (Germany), whereas HCV genotyping was carried out using AmpliSens[®] HCV-1/2/3-FRT kit from Amplisen (Russia).

Data were collected in a predesigned pro forma. All categorical data were expressed in percent and absolute numbers. All numerical continuous data were expressed in mean \pm SD. Data were entered in Microsoft Excel 2010 and extracted to SPSS version 20 (IBM Corp., Armonk, NY).

RESULTS

A total of 89 patients were detected with Hepatitis C virus infection during the study period. As per the exclusion criteria, finally 66 cases were taken up for the study (Figure 1).

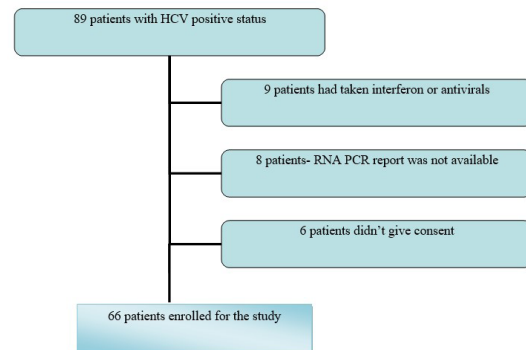


Figure 1: Flowchart showing study sample selection

Among the study subjects, 46 (69.7%) were male and 20 (30.3%) were female (M: F=2.3:1). The mean age of subjects was 34 \pm 10.42 years with a range of 21 – 65 years of age (Figure 2).

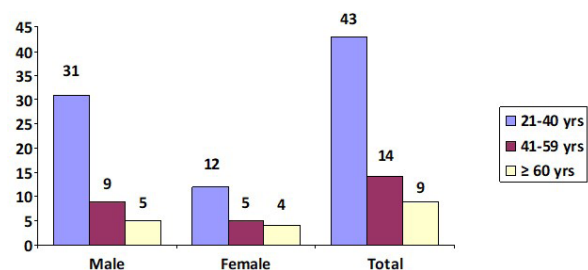


Figure 2: Age groups distribution of patients with Hepatitis C

The majority of study group comprised of 26 (39.4%) youngsters, aged below 30 years, who were jobless and were school or colleges drop-outs followed by 19 (28.8%) subjects who were running some local business. Five (7.6%) subjects were in government job and four (6%) were housewives. Rest 12 (18.2%) were either retired or farmers.

Majority, comprising of 44 (66.7%) were from rural areas whereas rest 22(33.3%) belonged to urban regions. Majority of patients (n=51, 72.7%) belonged to low to middle socioeconomic status.

Seventeen (25.8 %) patients were detected Hepatitis C on evaluation of jaundice and liver disease. Rest 49 (74.2%) patients had no signs and symptoms related to liver disease. Hepatitis C was detected in 16 (24.2%), nine (13.6%) and seven (10.6%) patients after serological evaluation during blood donation campaigns, foreign job recruitments and self blood investigation respectively. It was detected in 17(25.8%) patients prior to surgery, invasive procedures or antenatal visits during pregnancy.

Injecting drug use was the most common mode of infection for hepatitis C and seen in 39 (59.1%) patients. Blood transfusion,

haemodialysis and most probably sexual routes were the other modes of transmission. In seven (10.6%) patients, the exact mode of transmission could not be determined (Table 1).

Table 1: Risk factors/mode of transmission in patients with Hepatitis C (n=66)

Risk actors/mode of transmission	Number (%)
Intravenous drug use	39 (59.1%)
Blood transfusion	9 (13.6%)
Haemodialysis	4 (6.1%)
Unsafe sexual practices	3 (4.5%)
Spouse positive for Hepatitis C infection	2 (3.05%)
Tattooing	2 (3.05%)
Unidentified	7 (10.6%)

Most of the patients (n= 44; 66.7%) were asymptomatic, and had no clinical signs of liver diseases. The varied clinical presentation was as in table 2.

Table 2: Clinical presentation of patients with Hepatitis C (n=66)

Clinical presentation	Number (%)
No signs and symptoms	44 (66.7%)
Jaundice	18 (27.3%)
Ascites	12 (18.2%)
Variceal bleed	8 (12.1%)
Non specific symptoms	4 (6%)

Eighteen (27.3%) patients were diagnosed with HCV related cirrhosis of liver. Presentation with cirrhosis was observed more with male gender, and age >40 years (Table 3).

Table 3: HCV patients with cirrhosis (n=18)

Particulars	Number (%)	
Sex	Male	12 (66.7%)
	Female	6 (33.3%)
Age	<40 years	4 (22.2%)
	>40 years	14 (77.8%)

Five (7.6%) patients with hepatitis C were detected with HIV co infection, and three (4.5%) had HBV co infection. Liver enzymes were normal in around one third of the patients (n=21, 31.8%). Liver enzyme was raised (> 2x N) in 35 (68.2%) patients. Mean ALT and AST were 108±80.93 and 96±67.83 respectively.

HCV RNA was detected in all patients. High viral load (HCV RNA > 800,000 IU/ml) was detected in 28 (42.4%) patients. The mean HCV RNA was 1348,500 ±1052 IU/ml (range 2,000 to 50 million).

Genotype 3a was the most common, and seen in 41 (62.1%) patients followed by genotype 1a seen in 21 (31.8%) patients. Genotype 1b was seen in two (3.1%) patients and one (1.5%) patient was detected with genotype 6. No genotype could be identified in one (1.5%) patient. Genotype non identification was observed in the patient with lowest viral load (HCV RNA

=2,000 IU/ml)

All patients with high viral load (n=28) had either 3a or 1a genotypes. The various findings observed in common genotypes were as in table 4.

Table 4: Various findings with common genotypes

Particulars	Genotype 1a (n=21)	Genotype 3a (n=41)
Age 40 and below	12 (57.1%)	30 (73.2%)
Age > 40	9 (42.9%)	11 (26.8%)
Male	15 (71.4%)	27 (65.9%)
Female	6 (28.6%)	14 (34.1%)
Cirrhosis	6 (28.6%)	12 (29.3%)
Non cirrhosis	15 (71.4%)	29 (70.7%)
High viral load	9 (42.9%)	19 (46.3%)
Low Viral load	12 (57.1%)	22 (53.7%)

DISCUSSION

The mean age of study subjects was 34±10.42 years. Mean age was similar, 30.31 ± 6.68 years in a previous Nepalese study by Mishra et al.⁹ The majority of the study group comprised of patients aged below 40 years with male predominance in the current study. Similar were the findings by Bhaumik et al.¹⁰, Chakravarti et al.¹¹, and Gurubacharya et al.¹² All these studies reflect that patients usually acquire hepatitis C infection before 40 years of age. High risk behaviours including IV drug abuse which is greater in males compared to females in our society could be the most important factor in male predominance.

The majority of patients were from rural areas in the present study. Similar rural preponderance was reported by Bhaumik et al.¹⁰ Many of the patients were from rural areas and were staying away from their families in the current study.

The WHO updates in 2018 revealed that 60% of patients got infected through injecting drugs, 10% patients through blood transmission, 15% patients through sexual route, hemodialysis, and prenatal, other is 5% cases, and 10% remain unknown.¹ Injecting drug use was the primary risk factor for hepatitis C, accounting around two-third of new infections in 2016 in the United States.¹³ In the current study, injecting drug use was the most common risk factor for hepatitis C followed by a history of blood transfusion which was consistent with a previous Nepalese study by Gurubacharya et al.¹² Blood transfusion (30%) was the most common cause of hepatitis C transmission followed by injecting drugs in the other studies by Bhaumik et al.¹⁰ and Chakravarti et al.¹¹ respectively. In all the above studies, the common risk factors were the use of IV drugs or blood transfusions. In 10.6% of patients, the exact mode of transmission could not be determined in the current study. Similarly, the aetiology was obscure among 10.5% patients in the study by Gurubacharya et al.¹²

Co-infection with HIV was detected in three (4.5%) patients in the current study. Co-infection with HIV was detected in

5% and 10% patients in the studies by Bhaumik et al.¹⁰ and Chakravarti et al.¹¹ respectively. Patients with chronic hepatitis B or C should also be screened for HIV and vice versa as the modes of transmission are almost same.

Eighteen (27.3%) patients were diagnosed with HCV-related cirrhosis of the liver in the current study. Presentation with cirrhosis at the time of hepatitis C detection was lower (18%) in the study by Bhaumik et al.¹⁰ Our patients must have presented late with decompensation or were unaware about their hepatitis status.

Liver enzyme was raised (> 2x N) in 68.2% patients Mean ALT and AST were 108±80.93 and 96±67.83 respectively in the current study. Mean serum ALT and AST levels were 86.39 IU/mL ± 46.96 and 76.08 IU/mL ± 69.60 respectively according to Gurubacharya et al.¹² There should not be any hesitancy in screening for hepatitis in high risk group or sexually active age group with transaminitis or jaundice.

The mean HCV RNA was 13, 48,500 ±1052 in the present study whereas, it was 33,37,815 IU/mL ±5087752.64 by Gurubacharya et al.¹² Almost all untreated patients with Hepatitis C virus infection have high viral load (HCV RNA) .

Genotype 3a was the most common in the current study and seen in 62.1% of patients followed by genotype 1a seen in 31.8% of patients. Genotype 3a was similarly the most common genotypes according to Mishra et al.⁹ and Bhaumik et al.¹⁰ respectively. Genotype 3 was the most common genotype in previous published studies from India and Pakistan¹⁴⁻¹⁷ This could be due to the same geography and almost similar ethnic population in Indian sub continent. No genotype could be identified in one (1.5%) patient who had the lowest viral load in the current study. Genotype could not be identified in 16%

of HCV patients according to Ali et al.¹⁵. This non-identification could be due to low viral load or due to the possibility of a new genotype. Further study in this subject may give more insights. Viral load was significantly high in patients infected with HCV genotype 3 as compared to other genotypes in the studies by Mishra et al.⁹ and Ali et al.¹⁵ respectively. On the contrary Chakravarti et al.¹¹ had shown a significant higher HCV viral load in genotype 1. However, no such finding of higher viral load restricted to a genotype was observed in this study.

This study was carried out in a single-center with a small sample size. Treatment with directly acting antiviral (DAAs) agents according to different genotypes and response to therapy were not studied.

Serology tests during invasive procedures in hospital settings seem helpful in detecting patients with HCV infection. All patients with history of IV drug abuse, blood transfusions, and persistent jaundice with transaminitis should be screened for infective hepatitis. Early detection and treatment with anti virals can reduce the burden of disease as well as decrease morbidity and mortality associated with chronic hepatitis C.

CONCLUSION

The majority of chronic hepatitis C infected were young patients aged <40 years. Injecting drug use was the most common mode of infection. Most of the patients were asymptomatic and about one-fourth had cirrhosis of the liver at HCV detection. Hepatitis C virus RNA was detected in all patients. Genotype 3a was the most common, followed by genotype 1a in this region.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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