Original Article

Sustained virological response in HCV patients receiving antiviral treatment at a teaching centre of northern India

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Abstract

In India, it is estimated that 10–24 million people are living with active HCV infection, with a seroprevalence of 0.09% to 2.02% among the healthy population. The current study evaluates the efficacy of newer pan-genotypic directly acting antiviral drugs for SVR, which is the hallmark of successful HCV therapy. Data were collected on the prevalence of HCV infection, rates of SVR, and associated risk factors. In univariate analysis, serum albumin, AST, and APRI are significant predictors of SVR with $P < 0.05$. Specifically, a unit increase in serum albumin doubled the chances of achieving SVR (OR: 2.08, CI: 1.02–4.19), while increases in AST and APRI values were associated with reduced chances of SVR (OR: -0.99, CI: 0.98–0.99; OR: -0.79, CI: 0.64–0.98). Non-cirrhotic patients were significantly more likely to achieve SVR compared to decompensated cirrhotic patients (OR: 6.48, CI: 1.46–28.59). In the multivariable logistic regression analysis, taking all variables with a P value < 0.05 in the univariate analysis, such an association was not found, and it established the multifactorial nature of SVR. The present study underlines the importance of early diagnosis and the effectiveness of antiviral drugs against improved treatment outcomes of HCV patients in India. The findings present the challenges and successes in HCV elimination in a diverse and populous country.

Keywords: Albumin, APRI, cirrhosis, DAA, HCV, SVR, logistic regression, risk factors

Introduction

Hepatitis C virus (HCV) is a single-stranded RNA virus, which belongs to the Flaviviridae family.[1] HCV accounts for 15%–20% of cases of acute hepatitis approximately and around 50% to 80% of HCV patients will develop chronic infection following acute infection. There is a high risk of development of life-threatening complications in chronic hepatitis C (CHC) patients, such as cirrhosis in 20% of cases and hepatocellular carcinoma (HCC) at an incidence of 4%–5% per year in cirrhotic patients. HCV infects approximately 170 million individuals worldwide.[2] According to World Health Organization (WHO), approximately 10–24 million population is estimated to be living with active HCV infection in India and seroprevalence of HCV among healthy population has been estimated to be 0.09 to 2.02% in India.[3] The National Viral Hepatitis Control Program (NVHCP) was launched by the Government of India in 2018, on the occasion of World Hepatitis Day with the aim to combat hepatitis and achieve countrywide elimination of hepatitis C by 2030.[4] Early diagnosis of hepatitis C infection is critical for timely initiation of treatment and with the availability of newer class of safe, oral, and pan-genotypic directly acting antiviral drugs (DAAs) in the

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recent years, the treatment and cure of hepatitis C has become possible. The sustained virological response (SVR) has become the best indication of successful therapy for HCV infection and is labelled a surrogate therapeutic and clinically meaningful end point of successful antiviral therapy.[5]

The path to HCV elimination in India, a country with large population, various cultural practices, and diverse socioeconomic status, has presented with both challenges and success stories.[6] The present study was conducted to determine the prevalence of HCV infection, the percentage of patients achieving SVR with current antiviral therapy, and the assessment of the associated risk factors.

Procedure

Study design

This is a prospective study conducted in the Department of Microbiology of a teaching centre in northern India from 1st January 2022 to 31st December 2022 after obtaining ethical approval from the Institutional Ethics Committee.

Study population

Patients attending OPD (outpatient department) at our centre who were found positive for HCV antibody by rapid card test or enzyme-linked immunoassay test (ELISA) and had a detectable viral load, during the study period, formed the study population and a written informed consent was obtained from them for participating in the study. A total of 121 individuals with hepatitis C infection were enrolled after meeting the study criteria during the period and followed for at least 12 weeks post-treatment to evaluate for sustained virological response (SVR12). SVR12 was defined as an absence of detectable HCV RNA, 12 weeks after the completion of treatment.

Exclusion criteria

Individuals aged <16 years, coinfection by hepatitis B virus or human immunodeficiency virus, pregnant females, people with disseminated malignancy, advanced cardiovascular, neurological, or pulmonary disease with short life expectancy and those who refused to give consent, were not enrolled in the study.

Clinical and laboratory assessments

All patients were subjected to clinical assessment and complete history was recorded. Information was obtained about risk factors like history of blood transfusion, haemodialysis, any high-risk sexual behaviour, use of injection or other drugs, tattooing, occupational exposure to blood/body fluids, etc., The diagnosis of cirrhosis was based on the presence of stigmata of chronic liver disease, splenomegaly, ascites, history of hepatic encephalopathy, or variceal bleeding.

Initially, patients were tested for anti-HCV, HBsAg, and anti-HIV and other baseline laboratory investigations, like complete blood count (CBC), liver function tests (aspartate transaminase, alanine transaminase, serum bilirubin, serum albumin, and international normalized ratio), serum creatinine, and abdominal ultrasound, were done. The aspartate aminotransferase (AST)-to-platelet ratio index (APRI ≥ 2.0) or FIB-4 score (>3.25) was used to confirm the diagnosis of cirrhosis. FIB-4 was calculated [age (years) × AST (IU/l)/(platelet count (10^9/L) × √ALT (IU/L))] for all patients.[4] A quantitative HCV RNA measurement was performed using a commercially available Truenat™ HCV test, manufactured by Molbio Diagnostics Private Limited, which is a chip-based real-time reverse transcription polymerase chain reaction (RT-PCR) test based on Taqman chemistry, that is run on Truelab® Quattro real-time quantitative micro-PCR Analyser.[5] Viral load testing was done again after 12 weeks of completion of treatment to evaluate for SVR12.

Treatment

Patients who were found HCV antibody positive on rapid card test or ELISA and confirmed on quantitative polymerase chain reaction test for HCV RNA test, were put on oral antiviral treatment. Patients without cirrhosis (uncomplicated) were treated with Sofosbuvir (400 mg) and Daclatasvir (60 mg) for 12 weeks, patients with cirrhosis-compensated (Child–Pugh A) were treated with Sofosbuvir (400 mg) and Velpatasvir (100 mg) for 12 weeks, patients with cirrhosis-decompensated (Child–Pugh B and C) were treated with Sofosbuvir (400 mg), Velpatasvir (100 mg), and Ribavarin (600–1200 mg) for 12 weeks, while in Ribavarin intolerant patients—Sofosbuvir (400 mg) and Velpatasvir (100 mg) were given for 24 weeks. All patients were issued a 4-week supply of medicine at each visit and were requested to return five days before the next refill. Adherence to treatment was defined as no interruption in the treatment and the patient completing the prescribed duration of treatment.[4]

Statistical analysis

Data were analysed using SPSS 25 version. The characteristics of patients were presented as frequencies and percentages. An independent *t* test was used to find the significant difference between the continuous variables. Associations between SVR achievement status and risk factors were assessed using univariable and multivariable logistic regression analyses. Crude odds ratios, adjusted odds ratios, and 95% confidence intervals (CIs) were determined for each potential risk factor using logistic regression analysis, and the significance level was fixed at $P < 0.05$.

Results

A total of 121 patients were analysed for this study. The mean age of patients was 43.28 ± 14.49 years with a range of 16–72 years. The patients were categorized according to their age, approximately similar 26 (21.5%), 27 (22.3%), 28 (23.1%) patients were present in the age group 20–30 years, 40–50 years, 50–60 years, respectively. A little less 24 (19.8%) patients were between the age of 30 and 40 years. Very few 4 (3.3%) were ≤20 years patients, whereas more than 60 years were only

12 (9.9%) patients. A male preponderance was seen in the study subjects as 67 (55.4%) patients were male while 54 (44.6%) were females. As the teaching centre was located in Agra, maximum 79 (65.3%) HCV patients were from Agra only, 18 (14.9%) were from Mathura, and other patients were from nearby cities.

The disease stage of patients was also classified based on criteria, majority 74 (61.2%) were non-cirrhotic, 36 (29.2%) were compensated cirrhotic, and 11 (9.1%) were decompensated cirrhotic patients.[7] So accordingly, regime 1, regime 2, and regime 3 were given to non-cirrhotic, compensated cirrhotic, and decompensated cirrhotic patients, respectively. Among all the patients, maximum 44 (36.4%) patients reported occupational exposure to blood or body fluids as a risk factor for HCV followed by 42 (34.7%) patients with a history of receiving injection or surgery for therapeutic purposes. High-risk sexual behaviour was stated by 22 (18.2%) subjects, while 13 (10.7%) informed other risk factors of HCV. The patients were divided into two groups on the basis of SVR achievement, the patients who did not achieve SVR (Group A, n = 15) and who achieved SVR (Group B, n = 106).

The difference between the two groups was checked by using an independent *t* test. There were no statistically significant differences between the Group A patients and Group B patients in terms of age, weight, haemoglobin, serum bilirubin, PT INR, ALT, platelet count, serum creatinine, and eGFR, whereas there was a statistically significant difference in the levels of serum albumin, AST, APRI, FIB 4 among SVR-achieved and not achieved patients as presented in Table 1.

Logistic regression analysis

The dependent variable was SVR achievement status of HCV positive patients. The risk factors assessed included the participants age, weight, haemoglobin, serum albumin, serum bilirubin, PT INR, ALT, AST, platelet count, serum creatinine, eGFR, APRI, FIB-4, gender (male, female), stages of disease (decompensated cirrhotic, non-cirrhotic, compensated cirrhotic), high risk sexual behaviour (no, yes), history of receiving injection/surgery (no, yes), occupational exposure to blood/body fluids (no, yes), and others (no, yes). The results are presented in Table 2. As the outcome variable (SVR achieved) is divided into two groups, we used a binary logistic regression model to examine the association between SVR achievement status and independent variables while adjusting for other variables enumerated earlier in Table 1.

The results of the univariate analysis showed that serum albumin, AST, and APRI were statistically significant (*P* value < 0.05). If there is unit increase in serum albumin, there are two times more chances of achieving SVR (OR: 2.08, CI: 1.02–4.19), with the increase in the value of AST and APRI, the chance of SVR achievement is decreased (OR: -0.99, CI: 0.98–0.99), (OR: -0.79, CI: 0.64–0.98), respectively. Non-cirrhotic patients have six times more chances of achieving SVR (OR: 6.48, CI: 1.46–28.59) compared to decompensated cirrhotic patients.

Table 1: Comparison between the SVR-achieved patients and who do not achieve SVR

Variable	Group A Mean (*n*=15)	Group B Mean (*n*=106)	*P*
Age	47.80±15.49	42.64±14.31	>0.05
Weight	56.60±13.08	51.92±10.54	>0.05
Haemoglobin	11.41±2.77	11.41±2.49	>0.05
Serum albumin	3.45±0.81	3.86±0.68	<0.05
Serum bilirubin	1.08±0.96	0.72±0.81	>0.05
PT INR	1.40±3.51	0.70±2.23	>0.05
ALT	95.28±72.93	76.07±52.63	>0.05
AST	108.70±91.75	72.86±48.33	<0.05
Platelet count	292466.67±644836.28	164443.40±81530.72	>0.05
Serum creatinine	1.10±0.44	1.28±1.58	>0.05
eGFR	64.85±20.70	66.02±27.85	>0.05
APRI	4.74±7.93	1.63±1.67	<0.001
FIB-4	9.66±18.03	3.26±3.22	<0.001

Table 2: Univariable logistic regression analysis of risk factors for SVR achievement status

2A. Predisposing factors

Factor	*P*	Crude OR	95% CI for OR
Age	0.20	-0.98	0.93–1.01
Weight	0.12	-0.96	0.91–1.01
Gender			
Male	-	-	-
Female	0.14	2.46	0.73–8.20
Stages of disease			
Decompensated Cirrhotic	-	-	-
Non-cirrhotic	0.01*	6.48	1.46–28.59
Compensated cirrhotic	0.11	3.54	0.75–16.68
High-risk sexual behaviour			
No	-	-	-
Yes	0.37	-0.56	0.16–1.96
History of receiving injection/surgery			
No	-	-	-
Yes	0.08	3.94	0.84–18.36
Occupational exposure to blood/body fluids			
No	-	-	-
Yes	0.76	-0.84	0.27–2.53
Others			
No	-	-	-
Yes	0.23	-0.42	0.10–1.72

2B: Laboratory parameters

Factor	*P*	Crude OR	95% CI for OR
Haemoglobin	0.99	1.00	0.80–1.24
Serum albumin	0.04*	2.08	1.02–4.19
Serum bilirubin	0.18	-0.32	0.45–1.16
PT INR	0.32	-0.92	0.77–1.08
ALT	0.22	-0.99	0.98–1.00
AST	0.03*	-0.99	0.98–0.99
Platelet count	0.16	1.00	1.00–1.00
Serum creatinine	0.67	1.12	0.65–1.93
eGFR	0.88	1.00	0.98–1.02
APRI	0.03*	-0.79	0.64–0.98
FIB-4	0.06	-0.90	0.81–1.00

The associations between SVR achievement and risk factors were assessed using multivariable logistic regression analysis, all variables with a *P* value < 0.05 in the univariable analysis were included in the multivariable model. The variables in the final model were selected using stepwise procedures. We hypothesized that these variables would be associated with fewer chances of SVR achievement. The dependent variable was SVR status among hepatitis C infected recruited patients, results are reported in Table 3.

From the results of the multivariable analysis, it was revealed that no risk factor was significant. No associations were found between serum albumin, AST, APRI, and stages of disease with SVR. These findings demonstrate that SVR is multifactorial.

Discussion

The National Viral Hepatitis Control Program (NVHCP) launched by the Government of India aims to address the challenges posed by viral hepatitis through prevention, screening, diagnosis, treatment, and counselling services. The program synergizes with other national initiatives to improve resource utilization and enhance early treatment and prevention strategies. This study evaluates the effectiveness of antiviral therapies in achieving SVR among hepatitis C virus (HCV) patients and identifies risk factors associated with treatment outcomes. High-risk groups, including patients with HIV, those on haemodialysis, intravenous drug users, and individuals with high-risk sexual behaviour or attending STD clinics, have an HCV prevalence of 3.5%–44.7%. A study identified occupational exposure to blood or bodily fluids (36.45%) and history of injections or surgery (34.7%) as the main risk factors for HCV infection, with 18.2% of patients reporting high-risk sexual behaviour.[8]

The study conducted at our centre found that out of 121 HCV patients, 106 achieved SVR12, indicating an overall success rate of 87.6%. In comparison, the study by Pol *et al.*[9] reported a >90% SVR rate using a combination of Sofosbuvir and Daclatasvir in chronic HCV patients. Similarly, Ferenci *et al.*[10] noted higher SVR rates in patients with chronic hepatitis or Child-Pugh A liver cirrhosis compared to those with more severe cirrhosis (Child–Pugh B or C). These findings also corroborate the high antiviral potency and favourable outcomes of DAA regimens observed in the study by Soliman *et al.*[11] The analysis of factors affecting SVR achievement in the present study identified several key variables. Older age was significantly associated with lower SVR rates in multiple studies. The mean age of non-responders in our study was higher (47.80 ± 15.49 years) compared to responders (42.64 ± 14.31 years), however, this was not found to be significant. On the other hand, the study by Reid *et al.*,[12] indicates that advanced age may negatively impact treatment response due to longer infection duration and associated complications. The presence of cirrhosis, especially decompensated cirrhosis, was a significant predictor of non-response. Our study found that non-cirrhotic patients (OR: 6.48, CI: 1.46–28.59) had significantly higher chances of achieving SVR compared to decompensated cirrhotic patients. This finding is in line with other studies, where cirrhosis severity was inversely related to treatment success.[13,14] Lower platelet counts and serum albumin levels were associated with non-response to treatment. These factors indicate liver dysfunction, which adversely affects treatment outcomes. In our study, non-responders had lower serum albumin levels (3.45 ± 0.81 g/dL) compared to responders (3.86 ± 0.68 g/dL), and this was statistically significant ($P < 0.05$). Decrease in APRI was significantly related with SVR achievement in responders. Similarly, lower FIB-4 scores were found in group of responders. This was found to be consistent with other studies that have explored these non-invasive Markers' correlation with SVR12 in patients on DAAs.[15,16]

Table 3: Multivariable logistic regression analysis for SVR achievement status

Risk factor	*P*	Adj. OR	CI
Serum albumin	0.33	1.50	0.66–3.40
AST	0.83	0.99	0.98–1.01
APRI	0.37	0.85	0.60–1.20
Stages of disease			
Decompensated cirrhotic	-	-	-
Non-cirrhotic	0.43	2.16	0.31–14.80
Compensated cirrhotic	0.39	2.20	0.35–13.80

The findings of the multivariable logistic regression analysis for SVR achievement status are shown in the result section. The analysis shows that none of the evaluated risk factors were significantly associated with achieving SVR. The risk factors considered included serum albumin, AST, APRI, and disease stages (non-cirrhotic, compensated cirrhotic, and decompensated cirrhotic). For serum albumin, AST, and APRI, the *P* values and adjusted odds ratios (Adj. OR) with confidence intervals (CI) indicated no significant associations. Additionally, no significant differences were found between the cirrhotic disease stages (decompensated vs. compensated) and non-cirrhotic cases.

The multifactorial character of SVR accomplishment, as shown by the results, also suggests that the variables that are typically thought of as potential predictors did not significantly affect the results of this investigation. This shows that there is no one or a small number of factors that can be responsible for achieving SVR, underscoring the need for a more comprehensive understanding of the interactions between many factors that affect SVR. The exclusion of patients with co-infections (HBV, HIV), as well as those with advanced cardiovascular, neurological, or pulmonary diseases, and pregnant women, may have skewed the results towards a healthier population. Additionally, our study did not delve deeply into treatment adherence or the management of side effects, both of which are crucial for optimizing treatment outcomes. The findings from the present study align well with international studies, highlighting the effectiveness of DAA regimens in achieving high SVR rates. Future research should have broader patient inclusion to help generalize the findings

more effectively. They should also emphasize on ensuring patient adherence and addressing side effects as key components of improving therapeutic success.

Conclusion

The present study confirms worldwide data that direct-acting antiviral medications are effective in showing high rates of SVR in patients with hepatitis C virus infection. Although an overall outcome of SVR of 87.6% in our study is very encouraging, it is quite apparent that attainment of SVR is multifactorial in nature, as our multivariable analysis demonstrated that established risk markers, such as serum albumin, AST, APRI, and liver disease stages, were not meaningful predictors of the outcomes. This highlights the complexity of treatment responses and underscores the importance of gaining a more thorough understanding of the variables impacting SVR. The data showed that the predictors of non-response are advanced liver disease severity and advanced age, which identifies the need for timely detection and treatment. Hence, the NVHCP's integrated approach is better suited to improving treatment outcomes, expanding access, and ensuring continued care. The study underscores the importance of early diagnosis and treatment, particularly in non-cirrhotic patients and those with better liver function markers. The NVHCP's integrated approach is well positioned to leverage these insights, promoting early treatment and improving outcomes for HCV patients in India. These findings in turn must influence clinical and political decision-making processes in support of combating HCV while further nourishing better public health outcomes for India.

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Conflicts of interest

There are no conflicts of interest.

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