Original Article

SVR timelines in hepatitis - C irrespective of viral genotype: An Indian perspective

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Abstract

Background: Sustained Virologic Response (SVR) refers to successful hepatitis C treatment with undetectable HCV RNA. The duration to achieve SVR is typically 12 weeks globally, though this can vary depending on the viral genotype. Our prime objective in this study was to estimate the mean duration of SVR attainment among treatment-naïve hepatitis C individuals irrespective of viral genotype in India. **Materials and Methods:** A longitudinal observational study was done on 220 treatment-naïve hepatitis C patients from January 2022 to June 2024 at an Indian tertiary hospital. Patients were treated with 400 mg Sofosbuvir and 100 mg Velpatasvir (SOF/VEL), with HCV RNA measured at 8, 12, and 24 weeks to track SVR attainment. **Results and Observations:** Out of 220 patients, a total of 212 patients (96.3%) achieved SVR. Of these 84.9% attained SVR in 8 weeks, 11.7% in 12 weeks, and 3.3% in 24 weeks, with a mean duration of 9.22 ± 3.4 weeks. SVR achievement rates for Child-Pugh classes A, B, and C were 98.4%, 90%, and 62.5%, respectively. The majority of Child-Pugh class A patients achieved SVR in just 8 weeks, demonstrating a quicker treatment response. A high degree of concordance is observed between SVR12 and SVR24. **Conclusion:** Our findings suggest that hepatitis treatment duration varies based on Child-Pugh class and cirrhosis progression indicating the need for individualized treatment plans with tailored therapy durations. As most patients achieved SVR within 8 weeks, a shorter DAA regimen could be effective in the management of hepatitis C, warranting further research to optimize treatment timelines.

Keywords: Child-pugh class, direct-acting antivirals (DAA), hepatitis C, sofosbuvir/velpatasvir (SOF/VEL), sustained virologic response (SVR)

Introduction

Worldwide, approximately 50 million people are affected by chronic hepatitis C, with around 1 million new infections yearly. According to WHO estimates, about 242,000 people died from hepatitis C in 2022, with most deaths caused by cirrhosis and hepatocellular carcinoma (HCC).[1] An estimated 6 to 12 million people in India have chronic hepatitis C.[2] There are 8 recognized Hepatitis C Virus (HCV) genotypes globally, with genotype 1 as the most widespread worldwide, while genotype 3 is the most prevalent in India.[3] The development of pangenotypic drugs has eliminated the need for genotype testing. In accordance with the availability of these pangenotypic drugs, we assess the sustained virologic response (SVR) in our study irrespective of genotype.

Treatment efficacy, or the effectiveness of antiviral therapy in eliminating viral infection, is measured by the percentage of individuals who achieve SVR. SVR in hepatitis C refers to the outcome of antiviral treatment, where HCV RNA in the bloodstream becomes undetectable or falls below the minimum quantifiable level. After receiving therapy for 12–24 weeks, patients who attain SVR are often regarded as permanently

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cured. Individuals with SVR have a substantially lower rate of liver-associated disorders compared to those who do not respond to treatment. SVR rates could influence not just clinical results but also the financial and humanistic burdens associated with the illness. The duration to achieve SVR is typically 12 weeks globally, though this can vary depending on the viral genotype. The prime objective of this study was to determine the mean duration to achieve SVR in hepatitis C patients in India, regardless of genotype, given that most of the previous studies were conducted outside India. Our study focusing on the mean duration to achieve SVR in hepatitis C provides critical insights for both clinicians and patients. For healthcare providers, understanding the typical timeline for SVR attainment is essential in optimizing treatment protocols and managing patient expectations. It allows clinicians to promptly assess the effectiveness of therapy and make adjustments if needed, thereby ensuring better patient outcomes. For patients, being informed about the anticipated duration to reach SVR can alleviate anxiety and foster adherence, as it offers a clear sense of progress. This knowledge also empowers patients, motivating them to remain engaged in their treatment journey. Ultimately, such studies enhance shared decision-making, enabling both patients and clinicians to navigate the therapeutic process with greater confidence and clarity.

Materials and Methods

This longitudinal observational study was carried out on 220 treatment-naïve hepatitis C patients between January 2022 and June 2024 at a tertiary care hospital in India. We enrolled patients aged more than 14 years, from our Medicine outdoor and indoor who were newly diagnosed with hepatitis C, tested positive for anti-HCV antibodies, and had a detectable HCV RNA viral load. Patients with chronic liver disease (CLD) due to etiologies other than Hepatitis C [e.g., alcohol, hepatitis B, Metabolic dysfunction associated steatohepatitis/Metabolic dysfunction associated liver disease (MASH/MAFLD) and other causes] and those with other liver diseases like HCC, secondary metastasis, or other infective etiologies were excluded from the study. All the treatment experienced or treatment failure hepatitis C patients, those with coexisting Hepatitis B or HIV infection, and pregnant/lactating females were also excluded from the study. Informed consent was obtained from all individuals included in the study, and ethical approval was received from the Institutional Ethics Committee (SNMC/IEC/2024/294).

A detailed history was taken, documenting any evidence of hepatic encephalopathy (HE), upper gastrointestinal (UGI) bleeding, ascites other major complications, and prior hospitalizations. Laboratory tests, including a complete blood count, serum creatinine, liver function tests, and viral markers (HbsAg, Anti-HCV, HIV), were performed as part of the baseline assessment. Abdominal ultrasound was performed using our ESAOTE ultrasound machines, Model Mylab Class C (SR No. 4224) and Model Mylab Seven (SR No. 20243), to check for cirrhosis. Patients who tested positive for the Anti-HCV antibody went through further evaluation of HCV RNA viral load using the Truenat technique, utilizing our MOLBIO Truenat machine with the Trueprep AUTO v2 DNA/RNA extractor and the Truelab Quattro processing unit. All the individuals were enrolled under the National viral hepatitis control program (NVHCP) and were initiated on a DAA regimen comprising 400 mg of Sofosbuvir and 100 mg of Velpatasvir (SOF/VEL), in accordance with the national guidelines for the diagnosis and management of viral hepatitis. Patients in Child-Pugh class A received 12 weeks of antiviral therapy, while those in classes B and C were treated for 24 weeks. HCV RNA viral loads have been measured at 8, 12, and 24 weeks following the initiation of the DAA regimen. Individuals who exhibited undetectable viral RNA during any phase of the study were regarded as having achieved SVR. The mean SVR attainment duration for the entire group was determined using the individual durations of SVR achievement.

Statistical analysis

The collected data was organized in a Microsoft Excel sheet and processed using SPSS version 25.0 for analysis. The data was summarized using descriptive statistics including frequency, percentage, mean, and standard deviation. Inferential statistics such as the Chi-square test, *t*-test, and ANOVA were used to validate the significance of differences between groups. A P value of < 0.05 was considered statistically significant. The results were displayed in tabular and graphical formats.

Results and Observations

In our study, 41.4% of the 220 individuals were aged 31-40 years, making it the largest group. The next largest group was 41-50 years, comprising 35.9%, followed by 16.4% aged 30 or younger and 6.4% over 50 years [Figure 1]. The mean age of the study group has been recorded as 39.41 ± 7.7 years. The study comprised 148 male and 72 female participants. In our study, 68 individuals were suffering from liver cirrhosis [Figure 2]. The mean SGOT level was found to be 127.3 ± 65 U/L, while the mean SGPT level was 138.0 ± 80 U/L [Figure 3]. Out of the 220 patients, 192 (87.3%) were classified into Child-Pugh class A, 20 (9.1%) into class B, and 8 (3.6%) into class C [Figure 4].

SVR achievement rates for Child-Pugh classes A, B, and C were 98.4%, 90%, and 62.5%, respectively [Table 1]. The majority of Child-Pugh class A individuals achieved SVR in just 8 weeks, demonstrating a quicker treatment response. This data suggests that patients with better liver function (Class A) respond faster and more effectively to treatment, whereas those with more severe liver dysfunction (Class C) take longer and show a lower proportion of nondetectable HCV RNA [Figure 5].

A total of 212 patients (96.3%) achieved SVR, of which 84.9% attained SVR in 8 weeks, 11.7% in 12 weeks, and 3.3% in 24 weeks, with a mean duration of 9.22 ± 3.4 weeks [Table 2].

Discussion

Combination therapy with DAA for 8 to 24 weeks has proven to be extremely successful in treating HCV infection. As per

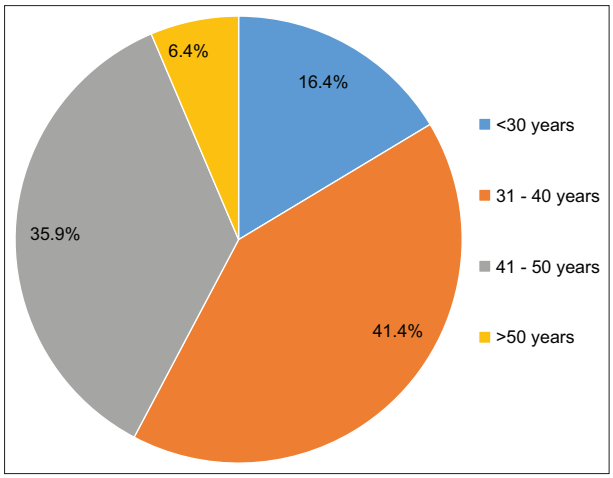

Figure 1: Distribution of the patients based on age group

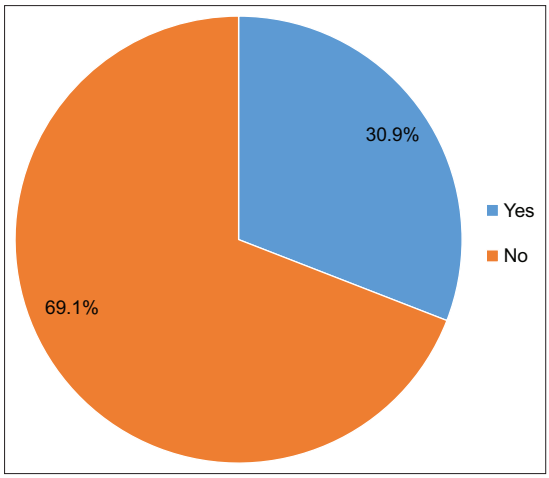

Figure 2: Distribution of the patients based on liver cirrhosis

Figure 3: Mean SGOT and SGPT Levels of the patients

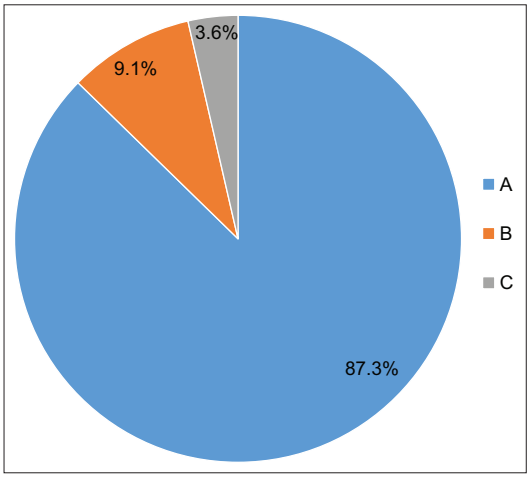

Figure 4: Distribution of the patients based on CHILD-PUGH class

existing guidelines, most patients are treated with 12 weeks of DAA treatment course, achieving high SVR rates across several viral or host factors. Nevertheless, evidence is mounting that several patients achieve SVR with a shorter treatment course. Reducing therapy duration might lower medical expenditure, minimize side effects, and enhance adherence to the regimen. Therefore, we estimated the average time to reach SVR to explore the potential for a shorter DAA regimen, based on the possibility of achieving SVR as early as 8 weeks. In our study, SVR was achieved in 84.9% of cases within 8 weeks, followed by 12 weeks in 11.7% and 24 weeks in 3.3%, with a mean duration of 9.22 ± 3.4 weeks to attain SVR. Our findings were consistent with those of Gane E *et al.*,[4] who documented that 58.8% of patients achieved SVR within 8 weeks, 39.1% within 12 weeks, and 2.1% within 16 weeks. The ION-3 trial of Kowdley KV *et al.*,[5] demonstrated that 202 individuals out of 215 with HCV genotype 1, who had no cirrhosis and were new to therapy, achieved SVR post 8-week course with ledipasvir and sofosbuvir, yielding a 94% SVR rate (95% CI 90–97). The HCV-TARGET cohort in Terrault NA *et al.*,[6] yielded similar success with 8 weeks of ledipasvir and sofosbuvir, resulting in SVR for 271 of 282 participants, representing a 96% rate (95% CI 93–98). In the POLARIS-2 trial,[7] 8 weeks of treatment with sofosbuvir, velpatasvir, and voxilaprevir led to SVR in 476 individuals out of 501 with HCV genotypes 1–6, including those having and not having cirrhosis and who had not previously received DAA therapy, resulting in a 95% SVR rate. While in the POLARIS-3 trial,[8] SVR has been achieved by 106 individuals out of 110 with HCV genotype 3 and cirrhosis, corresponding to a 96% SVR rate. The significant SVR rates seen with approved treatments suggest that a broad array of patients might be effectively treated in just 8 weeks, and shorter treatment durations could be possible for specific groups. While reducing treatment durations could decrease overall costs, it is crucial to make sure that this does not compromise treatment efficacy.

In our study, 30.9% of the 220 patients had liver cirrhosis, with the majority being in Child-Pugh class A (87.3%), followed by class B (9.1%) and class C (3.6%). This is consistent with Gane E *et al.*,[4] who found cirrhosis in 20.7% of 4,390 cases. In our study, 18.1% (40/220) of patients had compensated cirrhosis, with 72.5% achieving SVR at 8 weeks, 87.5% at 12 weeks, and 92.5% at 24 weeks. Our observations are consistent with Mangia Alessandra *et al.*,[9] who included 5552 patients, 20.7% of whom had compensated cirrhosis and achieved SVR rates of 97.9% with a 12-week SOF/VEL regimen. Likewise, Esteban Rafael *et al.*,[10] found that 91% of compensated cirrhosis patients reached SVR12 with the same regimen. Our study found that

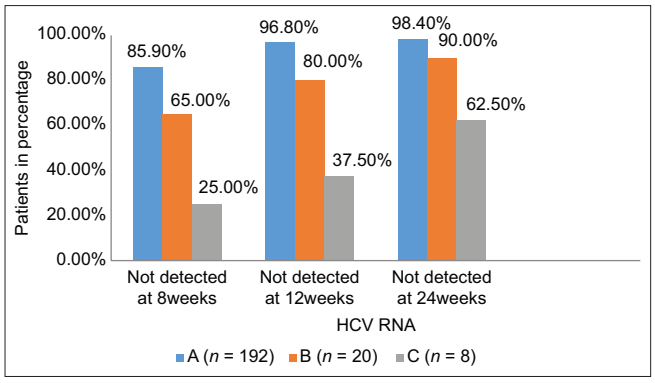

Figure 5: Comparison of the HCV RNA with Child Pugh class

Table 1: Comparison of the HCV RNA with Child-Pugh class

HCV RNA	CHILD-PUGH CLASS		
	A (*n*=192)	B (*n*=20)	C (*n*=8)
HCV RNA After 8 Weeks			
Not Detected	165 (85.93%)	13 (65.0%)	2 (25.0%)
Detected	27 (14.06%)	7 (35.0%)	6 (75.0%)
HCV RNA After 12 Weeks			
Not Detected	186 (96.8%)	16 (80.0%)	3 (37.5%)
Detected	6 (3.12%)	4 (20.0%)	5 (62.5%)
HCV RNA After 24 Weeks			
Not Detected	189 (98.4%)	18 (90.0%)	5 (62.5%)
Detected	3 (1.5%)	2 (10.0%)	3 (37.5%)

Table 2: Duration required to attain Sustained Virologic Response (SVR)

Duration to attain SVR	Number of patients (*n*=212)	Percentage
8 weeks	180	84.9
12 weeks	25	11.7
24 weeks	7	3.3
Mean duration to attain SVR	9.22±3.4	

12.7% (28/220) of patients had decompensated cirrhosis, with SVR rates of 53.5% at 8 weeks, 67.8% at 12 weeks, and 82.1% at 24 weeks. These results are consistent with MP Curry *et al.*,[11] who observed an 86% SVR24 rate in individuals having decompensated cirrhosis and received SOF/VEL regimen. Li JP *et al.*,[12] similarly reported that 60% of individuals having decompensated cirrhosis achieved SVR12 who received same treatment.

In our study, individuals with better liver function (Class A) respond more quickly and effectively to treatment, while those having extensive hepatic disorder (Class C) take longer and have lower rates of undetectable HCV RNA. Our study data reveals that SVR12 in our study was 96.8% for Child-Pugh class A, 80% for class B, and 37.5% for class C. Our results for Child-Pugh classes A and B are similar to those observed by Atsukawa *et al.*,[13] In their multicenter study of 12-week SOF/VEL treatment carried out across 33 institutions, the rates of SVR12 were 85.7% in class A, 97.9% in class B, and 88.2% in class C among 71 individuals having decompensated cirrhosis.

A retrospective multicenter cohort study in Brazil, involving 532 chronic hepatitis C patients treated with interferon-free regimens from November 2015 to November 2019, reported an overall ITT SVR of 92.6%. The participants had a mean age of 56.88 years, with 78.5% of them infected with HCV genotype 1, and 20.1% diagnosed with genotype 3. The most common treatment regimen consisted of Sofosbuvir (SOF) plus Daclatasvir, with or without ribavirin, accounting for 66.9% of the treatments. Sofosbuvir plus Simeprevir was the next most commonly used combination, administered to 21.2% of the cohort. The overall ITT SVR was 92.6% (493/532), and the m-ITT SVR was 96.8% (493/509). The findings of the Brazilian multicenter study, where 57.5% of the cohort presented with cirrhosis, some of whom had decompensated cirrhosis, are strikingly comparable to our own study population. In our cohort, 30.9% had cirrhosis, with a subset exhibiting decompensated cirrhosis. These similarities in patient characteristics strengthen the validity of our comparative analysis. Furthermore, our study achieved a remarkable 96.3% SVR rate with the use of interferon-free direct-acting antivirals (DAAs), aligning closely with the successful outcomes observed in the Brazilian study. The use of DAAs in both studies highlights their efficacy in treating hepatitis C, particularly in patients with advanced liver disease such as cirrhosis, underscoring their potential for achieving high rates of sustained virologic response in diverse patient populations.[14]

According to Gane E *et al.*,[4] more than 99% of individuals who attained SVR4 also achieved SVR12 in both the consistent and cumulative groups. The positive predictive value (PPV) of SVR4 for achieving SVR12 was unaffected by treatment duration. Both groups had a negative predictive value (NPV) of 100%, indicating that no patient who failed to reach SVR4 later achieved SVR12. Sensitivity was 100%, meaning every patient who reached SVR12 also attained SVR4. The specificity of SVR4 was 79.5%, allowing it to identify patients who did not achieve SVR12.

Our study results align with these findings, as 97.2% of patients who reached SVR8 also achieved SVR12, showing strong concordance between the two. The sensitivity was 66.67%, and specificity 85.37%, with a *P* value of <0.001 and a kappa value of 0.421 [Table 3]. Additionally, over 99% of patients who attained SVR12 also reached SVR24, indicating a high concordance between them, with a sensitivity of 75%, specificity of 95.75%, *P* value <0.001, and a kappa value of 0.732 [Table 4].

This study primarily aimed to evaluate the duration required for achieving sustained virologic response (SVR) in treatment-naïve hepatitis C patients in India, irrespective of viral genotype. What sets this study apart is its novelty, being the first Indian investigation to assess SVR8, a crucial marker for early virologic response. In contrast, most previous studies have predominantly focused on SVR12 and SVR24 endpoints, often targeting specific genotypes and conducted in international settings. This distinction not only highlights the unique scope of our study

Table 3: Comparison of the HCV RNA after 8 weeks with HCV RNA after 12 weeks

HCV RNA After 8 Weeks	HCV RNA After 12 Weeks		Total
	Detected	Not Detected	
Detected	10	30	40
Not Detected	05	175	180
Total	15	205	220

Table 4: Comparison of the HCV RNA after 12 weeks with HCV RNA after 24 weeks

HCV RNA After 12 Weeks	HCV RNA After 24 Weeks		Total
	Detected	Not Detected	
Detected	06	09	15
Not Detected	02	203	205
Total	08	212	220

but also contributes valuable insights into the dynamics of SVR achievement in the Indian population.

Conclusion

Our study found that most patients with Child-Pugh Class A achieved SVR in 8 weeks, while the majority with compensated cirrhosis attained it in 12 weeks and decompensated cirrhosis in 24 weeks, with the SOF/VEL regimen. Our findings suggest that hepatitis treatment duration varies based on Child-Pugh class and cirrhosis progression (no cirrhosis/compensated/decompensated), indicating the need for individualized treatment plans with tailored therapy durations.

While SVR12 remains the global standard, as seen even in our study where the majority of the patients with Child-Pugh class A and 80% of class B patients achieved SVR12, emerging evidence suggests that SVR may be achievable sooner. In our study, about 85% of patients reached SVR within 8 weeks, with a mean duration of around 9 weeks, indicating the potential for shorter DAA regimens in hepatitis C treatment. The high concordance between SVR8 and SVR12 suggests that a shorter SOF/VEL regimen could be effective, though more research is needed. These findings highlight the need for larger studies in Indian hepatitis C patients to explore shorter DAA timelines, potentially lowering costs and side effects. However, while shorter therapies are promising, risks like higher relapse rates, viral resistance, and patient loss to follow-up must be considered.

Ethical approval

The manuscript has been read and approved by all authors for whom the criteria of authorship have been met. The information provided is honest and true and is not disclosed on any forum elsewhere. Ethical approval was received from the Institutional Ethics Committee (SNMC/IEC/2024/294).

Study limitations

Our study encountered several limitations, notably a relatively small sample size and the absence of follow-up beyond 24 weeks. These constraints restricted our ability to evaluate relapse rates and assess long-term hepatic complications, such as alterations in Child-Pugh scores and liver fibrosis progression.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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