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STUDY OF THE SAFETY AND EFFICACY OF SOFOSBUVIR- VELPATASVIR COMBINATION IN HCV POSITIVE PATIENTS ON CLINICAL OUTCOME, VIRAL LOAD IN A TERTIARY CARE CENTRE.

General Medicine

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ABSTRACT

Hepatitis C virus (HCV) remains a significant public health concern globally, with a prevalence rate of approximately 1% worldwide and nearly 4.7 to 10.9 million affected individuals in India. The advent of direct-acting antivirals (DAAs) such as Sofosbuvir–Velpatasvir has revolutionized HCV management by achieving high sustained virologic response (SVR) rates across genotypes. This longitudinal observational study, conducted over 24 months in the Department of General Medicine at a tertiary care centre, aimed to evaluate the safety and efficacy of Sofosbuvir–Velpatasvir in 138 HCV-positive patients. Patients were evaluated using demographic, laboratory, and imaging parameters before and after a 12-week regimen. Viral load, liver function tests, and clinical outcomes were compared pre- and post-treatment. Results showed a significant reduction in mean HCV viral load from 379,832.77 ± 1,682,138.13 IU/ml to 191.05 ± 1,439.61 IU/ml ($p < 0.05$). The cure rate was 93.5%, with minimal adverse effects, primarily fatigue and headache. Both cirrhotic and non-cirrhotic groups demonstrated comparable cure rates. The findings reinforce the regimen's high efficacy and favourable safety profile, underscoring its utility in real-world tertiary care settings.

KEYWORDS

Hepatitis C virus, Sofosbuvir, Velpatasvir, Direct-acting antivirals, Sustained virologic response, Viral load reduction, Cirrhosis, Clinical outcomes, Tertiary care, Adverse effects.

INTRODUCTION

The hepatitis C virus was identified in 1989 following advances in cDNA cloning technology, ending years of uncertainty over the etiology of non-A, non-B hepatitis. It is a small, enveloped RNA virus of the Flaviviridae family, with seven known genotypes exhibiting geographical variation. Globally, the highest prevalence rates are in the Eastern Mediterranean and European regions, but India also bears a significant burden, with an estimated 4.7–10.9 million affected individuals.

Before the development of DAAs, treatment relied on pegylated interferon and ribavirin, which offered modest SVR rates (40–50% for genotype 1) and significant adverse effects. The approval of Sofosbuvir in 2013, followed by Velpatasvir in combination therapy, ushered in an era of highly effective, all-oral regimens with pan-genotypic coverage, simplified dosing, and minimal monitoring requirements.

Clinical trials such as ASTRAL-1 to ASTRAL-4 have demonstrated SVR rates above 95% in diverse patient populations, including those with compensated and decompensated cirrhosis. However, real-world data from tertiary care settings—where patients often present with advanced disease and comorbidities—are essential to validate these outcomes outside the controlled environment of clinical trials.

Aims And Objectives

Aim: To evaluate the safety and efficacy of the Sofosbuvir–Velpatasvir combination in hepatitis C virus (HCV)–positive patients by assessing its impact on clinical outcomes, viral load reduction, and treatment tolerability in a tertiary care setting.

Objectives:

1. To assess the efficacy of Sofosbuvir–Velpatasvir in reducing HCV viral load.
2. To evaluate the side effect profile of Sofosbuvir–Velpatasvir in treated patients.
3. To determine the clinical outcomes after three months of therapy.
4. To compare the effectiveness of Sofosbuvir–Velpatasvir between cirrhotic and non-cirrhotic patients before treatment initiation.

MATERIALS AND METHODS

Study Design And Setting:

- Longitudinal observational study conducted over 24 months in the Inpatient and Outpatient Departments of General Medicine at a tertiary care hospital.

Sample Size Calculation:

- Based on an expected efficacy rate (p) of 90%, allowable error (L) of 5%, and 95% confidence interval:

$$N = Z^2_{1-\alpha/2} \times p \times q / L^2$$

$$N = (1.96)2 \times 0.9 \times 0.1 / 0.052 = 138$$

Inclusion Criteria:

- Newly diagnosed HCV-positive patients.
- Age ≥ 14 years.

Exclusion Criteria:

- Patients on treatment for > 3 months.
- Age < 14 years.
- Co-infection with HBV.

Data Collection: Demographic details, MRD number, baseline laboratory parameters (HCV RNA titre, haemoglobin, platelet count, ALT, bilirubin, albumin), ultrasound findings, adverse effects, and clinical outcomes were documented. Post-treatment assessments were performed at 3 months.

Treatment Protocol:

- Sofosbuvir 400 mg + Velpatasvir 100 mg orally once daily for 12 weeks.

Statistical Analysis:

- Paired t-test for continuous variables, Chi-square test for categorical variables.
- $p < 0.05$ is considered statistically significant.

OBSERVATIONS AND RESULTS

This study presents a descriptive analysis of HCV-positive patients, focusing on the demographic profile and investigatory approach in newly diagnosed cases. The mean age of the study population (age range: 14–75 years) was 49.18 ± 12.47 years.

1. Age-wise Distribution Of HCV-positive Patients

Table 1: Age-wise Distribution Of Hcv-positive Patients With

Cirrhosis

Age (in years)	No of cases	Percentage (%)
≤ 20	5	3.62
21 – 30	6	4.34
31 – 40	21	15.21
41 – 50	36	26.08
51 – 60	46	33.33
61 – 70	18	13.04
> 70	6	4.34
Total	138	100

Interpretation:
HCV prevalence was highest in the **51–60-year** group (33.33%), followed by the **41–50-year group** (26.08%). Younger (≤30 years) and older (>70 years) groups had notably lower prevalence, indicating greater disease burden among middle-aged adults.

2. Gender-wise Distribution Of HCV-positive Patients
Table 2: Gender Wise Distribution Of Cases In HCV-positive Patients With Cirrhosis.

Gender	No. of Cases
Female	40
Male	98
Grand Total	138

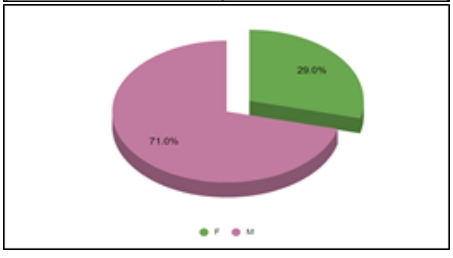

Figure 1: Gender wise distribution of Cases in HCV-positive patients with cirrhosis.

Interpretation:
Among the 138 cases, males constituted 71% and females 29%, indicating a significantly higher prevalence in males (Chi-square = 24.38, df = 1, $p = 1\times10^{-6}$).

3. Viral Load Reduction Following Sofosbuvir–Velpatasvir Therapy
Table 3: HCV Viral Load At Detection And After 3 Months Of Treatment

	Mean ± SD	Paired t-test
HCV viral load at detection	379832.77 ± 1682138.13	p = 0.0089
HCV viral load detection after 3 months of treatment.	191.05 ± 1439.61	

Interpretation:
After three months of treatment, the mean HCV viral load decreased from 379,832.77 to 191.05 IU/ml, a statistically significant reduction (p = 0.0089), demonstrating the high antiviral efficacy of Sofosbuvir–Velpatasvir.

4. Adverse Effects of Sofosbuvir–Velpatasvir
Table 4: Adverse Effects In HCV-positive Patients Treated With Sofosbuvir–Velpatasvir

ADVERSE EFFECTS	No. of cases	Percentage (%)
FATIQUE	12	8.695652174
FEVER	9	6.52173913
HEADACHE	10	7.246376812
NAUSEA	1	0.7246376812
NO COMPLAINTS	102	73.91304348
VOMITING	4	2.898550725
Grand Total	138	100

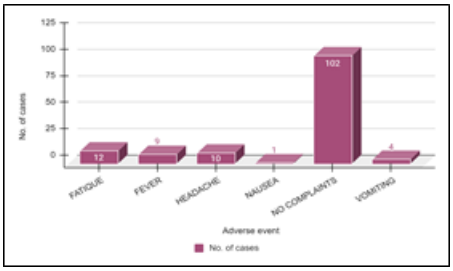

Figure 2: Adverse effects of sofosbuvir and Velpatasvir.

Interpretation:
The majority of patients (73.9%) reported no adverse effects. The most common reported symptom was fatigue (8.7%), followed by headache (7.2%) and fever (6.5%). Nausea and vomiting occurred in less than 3% of cases. The goodness-of-fit chi-square test ($\chi^2 = 329.22$, df = 5, $p < 0.001$) indicated that the distribution of adverse effects was highly significant.

5. Clinical Outcomes at 3 Months Post-treatment
Table 5: Clinical Outcomes of HCV-positive Patients Treated with Sofosbuvir–Velpatasvir

Clinical outcome at 3 months	No. of cases	Chi-Square test of Goodness of fit
Cured	129	Chi square = 104.3478
Relapse	9	df = 1
Total	138	p = 0

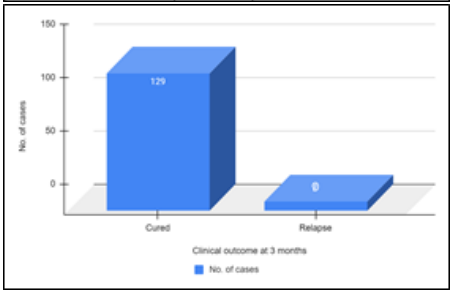

Figure 3: Clinical Outcomes Of HCV-positive patients treated with Sofosbuvir–Velpatasvir.

Interpretation:
At three months post-treatment, 93.5% of patients achieved a cure, while 6.5% experienced relapse. The chi-square test ($\chi^2 = 104.35$, df = 1, $p < 0.001$) confirmed the outcome distribution was highly significant, indicating strong treatment effectiveness.

6. Effectiveness of Sofosbuvir–Velpatasvir in Cirrhotic and Non-cirrhotic Patients
6.a: Baseline Characteristics Of Cirrhotic Patients
Table 6.a: Baseline Characteristics Of Cirrhotic Patients

Variables	Mean ± Std. deviation
HCV titre at detection (IU/ml)	2724245.49 ± 2360331.84
Hb (gm/dl)	11.01 ± 1.71
Platelet count (/ml)	318.49 ± 293.75
ALT (IU/L)	58.57 ± 26.71
Bilirubin (mg/dl)	1.01 ± 0.68
Albumin (gm/dl)	3.17 ± 0.28

Interpretation:
Cirrhotic patients presented with high baseline HCV viral loads and mild anemia. Platelet counts showed wide variability, consistent with liver-related hematological changes. Elevated ALT levels indicated hepatic inflammation, while near-normal bilirubin and moderately reduced albumin suggested relatively preserved liver synthetic function at baseline.

6.b: Baseline Characteristics Of Non-cirrhotic Patients
Table 6.b: Baseline Characteristics Of Non-cirrhotic Patients

Interpretation:
Non-cirrhotic patients had lower baseline HCV viral loads than cirrhotics, with mild anemia and moderately reduced platelet counts. ALT, bilirubin, and albumin values were largely normal, reflecting preserved liver function at presentation.

6.c: Post-treatment Characteristics of Cirrhotic Patients (After 3 Months)

Table 6.c: Post-treatment Characteristics of Cirrhotic Patients (After 3 Months)

Variables	Mean ± Std. deviation
HCV titre at detection (IU/ml)	195.30 ± 1455.34
Hb (gm/dl)	11.25± 1.50
Platelet count (per/ml)	174.70 ± 48.42
ALT (IU/L)	23.26 ± 8.61
Bilirubin (mg/dl)	0.57 ± 0.32
Albumin (gm/dl)	3.19 ± 0.37

Interpretation:
After 3 months of therapy, cirrhotic patients showed a marked viral load reduction with improved ALT levels, indicating reduced liver inflammation. Hemoglobin rose slightly, platelet counts stabilized, and bilirubin and albumin remained within healthy ranges, reflecting preserved liver function post-treatment.

6.d: Post-treatment Characteristics of Non-cirrhotic Patients (After 3 Months)

Table 6.d: Post-treatment Characteristics of Non-cirrhotic Patients (After 3 Months)

Variables	Mean ± Std. deviation
HCV titre at detection (IU/ml)	191.05 ± 1454.34
Hb (gm/dl)	11.25± 1.49
Platelet count (per/ml)	175.29 ± 48.28
ALT (IU/L)	23.31 ± 8.56
Bilirubin (mg/dl)	0.56 ± 0.32
Albumin (gm/dl)	3.18 ± 0.28

Interpretation:
Non-cirrhotic patients also achieved a marked decline in HCV viral load after treatment. Hemoglobin and platelet counts remained stable, and ALT levels decreased, indicating reduced liver inflammation. Bilirubin and albumin levels stayed within normal ranges, reflecting maintained liver function.

6.e: Subgroup Analysis of Cirrhotic Patients – Baseline vs. Post-treatment (3 Months)

Table 6.e: Subgroup Analysis of Cirrhotic Patients – Baseline vs. Post-treatment (3 Months)

Variables	Mean ± Std. deviation at detection.	Mean ± Std. deviation After 3 months of treatment.	Paired t-test
HCV titre (IU/ml)	2724245.49 ± 2360331.84	195.30 ± 1455.34	p < 0.05
Hb (gm/dl)	11.01 ± 1.71	11.25± 1.50	p < 0.05
Platelet count (/ml)	318.49 ± 293.75	174.70 ± 48.42	p = 1.9005
ALT (IU/L)	58.57 ± 26.71	23.26 ± 8.61	p < 0.05
Bilirubin (mg/dl)	1.01 ± 0.68	0.57 ± 0.32	p < 0.05
Albumin (gm/dl)	3.17 ± 0.28	3.19 ± 0.37	p = 0.0100

Interpretation:
Cirrhotic patients showed a significant decline in viral load and ALT levels after treatment, indicating effective viral suppression and reduced liver inflammation. Hemoglobin and bilirubin improved, albumin increased slightly, and platelet counts decreased, but without a significant change.

6.f: Subgroup Analysis of Non-cirrhotic Patients – Baseline vs. Post-treatment (3 Months)

Table 6.f: Subgroup Analysis of Non-cirrhotic Patients – Baseline

Variables	Mean ± Std. deviation at detection.	Mean ± Std. deviation After 3 months of treatment.	Paired t-test
HCV titre (IU/ml)	379832.77 ± 168213	195.30 ± 1455.34	p < 0.05
Hb (gm/dl)	10.97 ± 1.67	11.25± 1.50	p < 0.05
Platelet count (/ml)	176.42 ± 64.83	174.70 ± 48.42	p < 0.05
ALT (IU/L)	24.85 ± 12.95	23.26 ± 8.61	p = 3.1750
Bilirubin (mg/dl)	0.60 ± 0.48	0.57 ± 0.32	p = 0.0292
Albumin (gm/dl)	3.14 ± 0.34	3.17 ± 0.28	p = 3.0735

Interpretation:
Non-cirrhotic patients experienced a **significant viral load reduction** with mild improvements in hemoglobin and bilirubin. Platelet counts and ALT changes were minimal, and albumin remained stable, indicating preserved liver function post-treatment.

DISCUSSIONS

Hepatitis C virus (HCV) infection remains a major public health challenge worldwide, with significant implications for liver-related morbidity and mortality. In this study, we evaluated the clinical, virological, and biochemical outcomes of Sofosbuvir–Velpatasvir (SOF–VEL) therapy in HCV-positive patients, including both cirrhotic and non-cirrhotic cases, at our tertiary care centre.

1. Demographic Characteristics

The mean age of patients was 49.18 ± 12.47 years, with the highest prevalence in the 51–60 age group (33.33%), followed by 41–50 years (26.08%). Male predominance (71%) was statistically significant, consistent with studies by Khemnark et al. [13] and Shah et al. [30].

2. Antiviral Efficacy

SOF–VEL therapy significantly reduced HCV viral load in both cirrhotic and non-cirrhotic patients. Cirrhotic cases showed a drop from 2,724,245.49 IU/ml to 195.30 IU/ml, while non-cirrhotic cases reduced from 379,832.77 IU/ml to 191.05 IU/ml ($p < 0.05$). These results align with global SVR rates exceeding 90%.

3. Hematological And Biochemical Response

Post-treatment, hemoglobin levels improved slightly in both groups, while ALT and bilirubin levels decreased significantly, indicating reduced liver inflammation and improved function. Albumin levels showed mild improvement, suggesting better synthetic function. Platelet counts remained largely unchanged in cirrhotics, likely due to persistent hypersplenism.

4. Adverse Effects

The regimen was well-tolerated; 73.91% reported no side effects. Fatigue (8.70%), headache (7.25%), and fever (6.52%) were the most common, comparable to Anna LZ et al. [15].

5. Treatment Outcomes

After 3 months, 93.48% achieved a cure, with only 6.52% relapsing. These results are consistent with findings by Jeong Heo et al. [12], highlighting SOF–VEL's high efficacy and tolerability in both cirrhotic and non-cirrhotic patients, even in resource-limited settings.

CONCLUSION

This study evaluated HCV-positive patients, focusing on demographics, treatment outcomes, and side effects of Sofosbuvir–Velpatasvir therapy. Most patients were middle-aged, with the highest prevalence in the 51–60-year group (33.33%), and males predominated (71%). Treatment significantly reduced mean viral load from 379,832.77 ± 1,682,138.13 IU/ml to 191.05 ± 1,439.61 IU/ml ($p = 0.0089$), achieving a 93.5% cure rate. Only 6.5% of patients relapsed. Adverse effects were uncommon, with 73.91% reporting none. Fatigue, headache, and fever were the most frequent, while nausea and vomiting were rare. Cirrhotic patients showed marked improvements in viral load, ALT, and bilirubin, though platelet counts remained unchanged. Non-cirrhotic patients also had significant viral suppression with stable liver function. Overall, Sofosbuvir–Velpatasvir proved highly effective, well-tolerated, and applicable to both cirrhotic and non-cirrhotic HCV cases, underscoring its role as a first-line therapy.

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