Health Dynamics
eISSN: 3006-5518
Publisher: Knowledge Dynamics
DOI: https://doi.org/10.33846/hd30304

Original Research

Effect and Safety of Sofosbuvir and Daclatasvir in the Treatment of Hepatitis C Virus Infection Among Yemeni Patients Who Are Undergoing Hemodialysis

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Article history
Received: 6 February 2026
Revised: 14 March 2026
Accepted: 16 March 2026
Published Online: 31 March 2026

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How to cite this article: Al-Tayar BA, Sharif SE, Al-Tayar BA, Kassim A. Effect and Safety of Sofosbuvir and Daclatasvir in the Treatment of Hepatitis C Virus Infection Among Yemeni Patients Who Are Undergoing Hemodialysis. *Health Dynamics*, 2026, 3(3), 108-115. https://doi.org/10.33846/hd30304

ABSTRACT

Background: Hepatitis C virus (HCV) infection remains one of the most frequently acquired infections among patients undergoing hemodialysis and is associated with substantial morbidity and progressive liver disease. In Yemen, evidence regarding the efficacy and safety of direct-acting antivirals (DAAs) in this population remains limited. This study aims to evaluate the effectiveness and safety of a combination regimen of sofosbuvir and daclatasvir in treating HCV infection among Yemeni patients undergoing hemodialysis. **Methods:** This prospective study included 28 Yemeni patients with confirmed HCV infection who were receiving maintenance hemodialysis between January 2023 and December 2024. The study was conducted in the dialysis unit of Al-Gomhori Hospital in Taiz City, Yemen. All patients received sofosbuvir (400 mg) and daclatasvir (60 mg) three times weekly for 12 weeks. Virological response was assessed using HCV RNA PCR at baseline, at the end of treatment to determine early virological response (EVR), and 12 weeks after treatment completion to assess sustained virological response (SVR12). **Results:** The study population comprised 14 males (50%) and 14 females (50%), with a mean age of 44 ± 12 years. At baseline, most patients (75%) had a low viral load, while 21% had a high viral load and 4% had a moderate viral load. EVR was achieved in 25 patients (89.3%). One patient (3.6%) had persistent detectable HCV RNA, one patient (3.6%) discontinued treatment due to adverse effects, and one patient (3.6%) died during the study period. Among patients who completed therapy, SVR12 was achieved in all cases (100%). **Conclusion:** The combination of sofosbuvir and daclatasvir administered three times weekly appears to be an effective and well-tolerated treatment option for HCV infection in patients undergoing hemodialysis in resource-limited settings.

Keywords: Sofosbuvir; daclatasvir; hepatitis C virus; hemodialysis; direct-acting antivirals

1. INTRODUCTION

Hepatitis C virus (HCV) infection remains a significant global health challenge and a leading cause of chronic liver disease, including cirrhosis, hepatocellular carcinoma, and liver-related mortality. According to recent estimates,

approximately 58 million individuals worldwide are chronically infected with HCV, highlighting the persistent burden of this infection despite advances in antiviral therapy.[1]

Patients undergoing maintenance hemodialysis (MHD) represent a particularly vulnerable population, with a disproportionately high prevalence of HCV infection compared to the general population. This increased susceptibility is primarily attributable to repeated vascular access, frequent exposure to blood products, prolonged healthcare contact, and the risk of nosocomial transmission within dialysis units.[2] Consequently, HCV is recognized as the most common hepatotropic viral infection among patients receiving long-term hemodialysis. The reported prevalence in this population varies widely, ranging from 6% to 60% across different regions, reflecting disparities in infection control practices, screening strategies, and healthcare infrastructure.[3]

Nosocomial transmission remains a critical factor in sustaining HCV infection within dialysis settings, often linked to inadequate sterilization procedures, lapses in infection control, and cross-contamination during vascular access management.[4] Beyond increased exposure risk, patients on hemodialysis also experience more aggressive disease progression, with a higher likelihood of developing cirrhosis, hepatocellular carcinoma, and liver-related mortality compared to non-dialysis populations.[5] These compounded risks underscore the urgent need for safe and effective antiviral therapies tailored to this high-risk group.

Historically, the management of HCV infection in patients with advanced renal impairment relied on interferon-based regimens, either as monotherapy or in combination with ribavirin. However, these treatments were limited by suboptimal sustained virological response (SVR) rates, prolonged treatment duration, and poor tolerability, particularly in patients undergoing hemodialysis. Adverse effects such as anemia, fatigue, and flu-like symptoms often led to treatment discontinuation, thereby reducing overall effectiveness.[6] As a result, many patients with end-stage renal disease (ESRD) were historically undertreated or excluded from antiviral therapy.

The advent of direct-acting antivirals (DAAs) has dramatically transformed the treatment landscape of HCV infection, achieving SVR rates exceeding 90% with shorter treatment durations and improved safety profiles.[7] Despite these advances, the application of DAAs in patients with severe renal impairment remains complex. Sofosbuvir, a nucleotide analog inhibitor targeting the NS5B RNA-dependent RNA polymerase, has demonstrated high efficacy across multiple HCV genotypes. However, its use in patients with reduced renal function has been approached with caution due to the renal clearance of its inactive metabolite (GS-331007), which may accumulate in patients with impaired kidney function.[8] Although pharmacokinetic studies have raised concerns regarding potential toxicity at elevated metabolite levels, the clinical implications of this accumulation remain incompletely understood.

Current international guidelines recommend alternative DAA regimens, such as glecaprevir/pibrentasvir and grazoprevir/elbasvir, for patients with chronic hepatitis C and severe renal impairment or ESRD, given their favorable pharmacokinetic profiles in this population.[9] Nevertheless, access to these regimens is often limited in low-resource settings, including Yemen, where healthcare constraints restrict the availability of recommended therapies. This gap between guideline recommendations and real-world accessibility necessitates the evaluation of alternative, locally available treatment strategies.

Daclatasvir, an NS5A inhibitor predominantly metabolized by the liver, offers a pharmacologically suitable option for patients with renal impairment due to its minimal dependence on renal clearance. When combined with sofosbuvir, it provides dual inhibition of viral replication through complementary mechanisms targeting NS5A and NS5B proteins. Emerging evidence suggests that such combinations may remain effective even in patients with ESRD, particularly when dosing strategies are adapted to mitigate drug accumulation while maintaining antiviral efficacy.[8,10]

Despite growing global evidence supporting the use of DAAs in patients with renal impairment, data from Yemen remain scarce, particularly among patients undergoing hemodialysis. Given the high prevalence of HCV infection in this population and the limited availability of recommended antiviral regimens, there is a critical need for context-specific clinical evidence to guide treatment strategies.

Therefore, the present study was designed to evaluate the effectiveness and safety of a combination regimen of sofosbuvir and daclatasvir in the treatment of HCV infection among Yemeni patients undergoing maintenance hemodialysis.

2. METHODS

2.1 Sample Selection and Procedures

This prospective observational study was conducted to evaluate the effectiveness and safety of antiviral therapy under routine clinical conditions. The study was carried out in the dialysis unit of Al-Gomhori Hospital, a tertiary care center located in Taiz City, Yemen, which provides maintenance hemodialysis services to patients with end-stage renal disease (ESRD). Data collection was performed over two years, from January 1, 2023, to December 31, 2024.

The study population comprised adult patients undergoing maintenance hemodialysis with confirmed hepatitis C virus (HCV) infection. Diagnosis was established through positive anti-HCV antibody testing and confirmed by quantitative HCV RNA polymerase chain reaction (PCR). Patients were recruited during their routine dialysis sessions.

Participants were eligible for inclusion if they met the following criteria: age ≥18 years; confirmed HCV infection with a positive HCV RNA PCR test; receiving regular hemodialysis for ESRD (glomerular filtration rate <30 mL/min/1.73 m^2); and willingness to participate in the study. Patients were excluded if they were younger than 18 years, had co-infection with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), had chronic kidney disease not yet requiring hemodialysis, or had a history of previous treatment failure with direct-acting antiviral agents.

All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Ethical approval for the study was granted by the Ethical Committee of the Faculty of Medicine, Taiz University, Taiz, Yemen.

A total of 28 patients were included in the study. The sample size was determined based on the number of eligible patients attending the dialysis unit during the study period who met the inclusion criteria and consented to participate. Given the limited population of patients with concurrent HCV infection undergoing maintenance hemodialysis in the study setting, a convenience sampling approach was employed.

2.2 Treatment Protocol

All enrolled patients received a combination regimen of sofosbuvir (400 mg) and daclatasvir (60 mg), administered three times weekly for a duration of 12 weeks. The dosing schedule was adjusted to coincide with dialysis sessions and to minimize potential drug accumulation in patients with impaired renal function. All patients were followed for 12 weeks after the completion of treatment to assess SVR12. Clinical monitoring continued during this period to detect any delayed adverse events or virological relapse.

2.3 Clinical and Laboratory Assessment

At baseline, quantitative HCV RNA PCR testing was performed to confirm infection and determine viral load. Viral load was categorized as follows:

Low: 60–1,000,000 copies/mL;

Moderate: 1,000,000–2,000,000 copies/mL; and

High: >2,000,000 copies/mL

During the treatment period, patients were monitored regularly at each dialysis session. Clinical evaluations were conducted to assess general condition and identify any adverse events. Routine hematological and biochemical investigations were performed as part of standard clinical follow-up. Patients were encouraged to report any symptoms or treatment-related side effects.

2.4 Outcome Measures

The primary outcomes of the study were:

Early Virological Response (EVR): Undetectable HCV RNA by PCR at the end of 12 weeks of treatment; and

Sustained Virological Response (SVR12): Undetectable HCV RNA 12 weeks after completion of therapy.

2.5 Data Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 26. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The Shapiro–Wilk test was used to assess the normality of continuous variables. A p-value of <0.05 was considered statistically significant.

3. RESULTS

A total of 28 patients with confirmed HCV infection undergoing maintenance hemodialysis were included in the study (Table 1). The cohort comprised 14 males (50.0%) and 14 females (50.0%), indicating an equal gender distribution (Figure 1). The age of participants

ranged from 18 to 70 years, with a mean age of 44 ± 12 years.

Table 1. Descriptive statistics of the study population (n = 28)

Variable	Value
Sex, n (%)	
Male	14 (50.0)
Female	14 (50.0)
Age (years)	
Mean ± SD	44 ± 12
Range	18–70

3.1 Baseline Virological Profile

At baseline, all patients had detectable HCV RNA (Table 2). The mean viral load was 3.65×10^7 copies/mL (SD: 1.54×10^8), reflecting substantial inter-individual variability. Viral load values ranged from 260 to 8.11×10^8 copies/mL.

When categorized, most patients (75.0%, n = 21) had a low viral load, while 21.4% (n = 6) had a high viral load. Only one patient (3.6%) exhibited a moderate viral load (Table 3 and Figure 2).

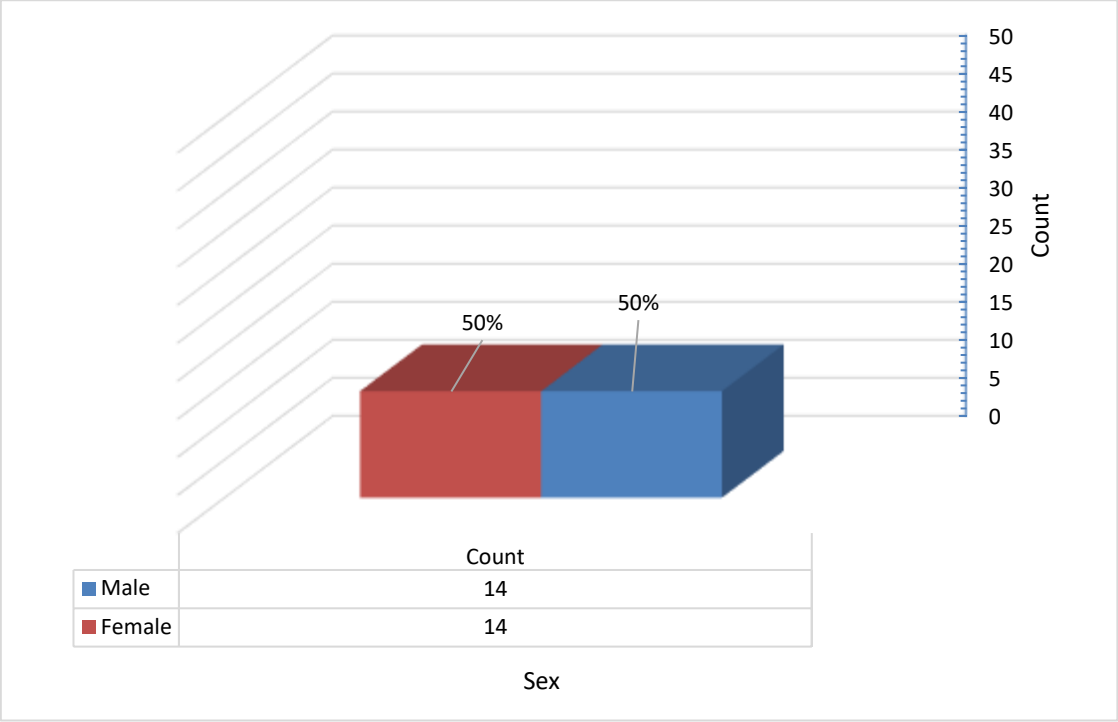

Figure 1. Sex distribution

Table 2. Baseline HCV RNA levels (copies/mL)

Parameter	Value
Mean	3.65×10^7
Standard deviation	1.54×10^8
Minimum	260
Maximum	8.11×10^8

Table 3. Distribution of baseline viral load categories

Viral Load Category	n (%)
Low	21 (75.0)
Moderate	1 (3.6)
High	6 (21.4)

3.2 Early Virological Response (EVR)

At the end of the 12-week treatment period, early virological response (EVR), defined as undetectable HCV RNA, was achieved in 25 out of 28 patients (89.3%; 95% CI: 71%–98%).

Among the remaining patients, one patient (3.6%) had persistent detectable HCV RNA, one patient (3.6%) discontinued treatment due to adverse effects, and one patient (3.6%) died during the study period (Table 4 and Figure 3).

Table 4. Early virological response (EVR) outcomes (n = 28)

Outcome	n (%)
Undetectable HCV RNA (EVR)	25 (89.3)
Detectable HCV RNA	1 (3.6)
Treatment discontinued (adverse effect)	1 (3.6)
Death	1 (3.6)

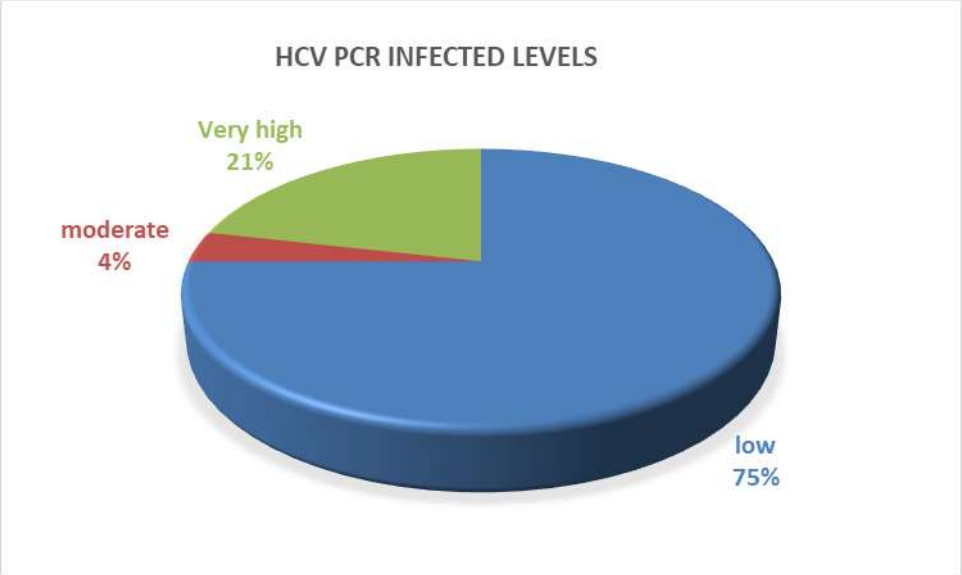

Figure 2. Pretreatment HCV RNA levels

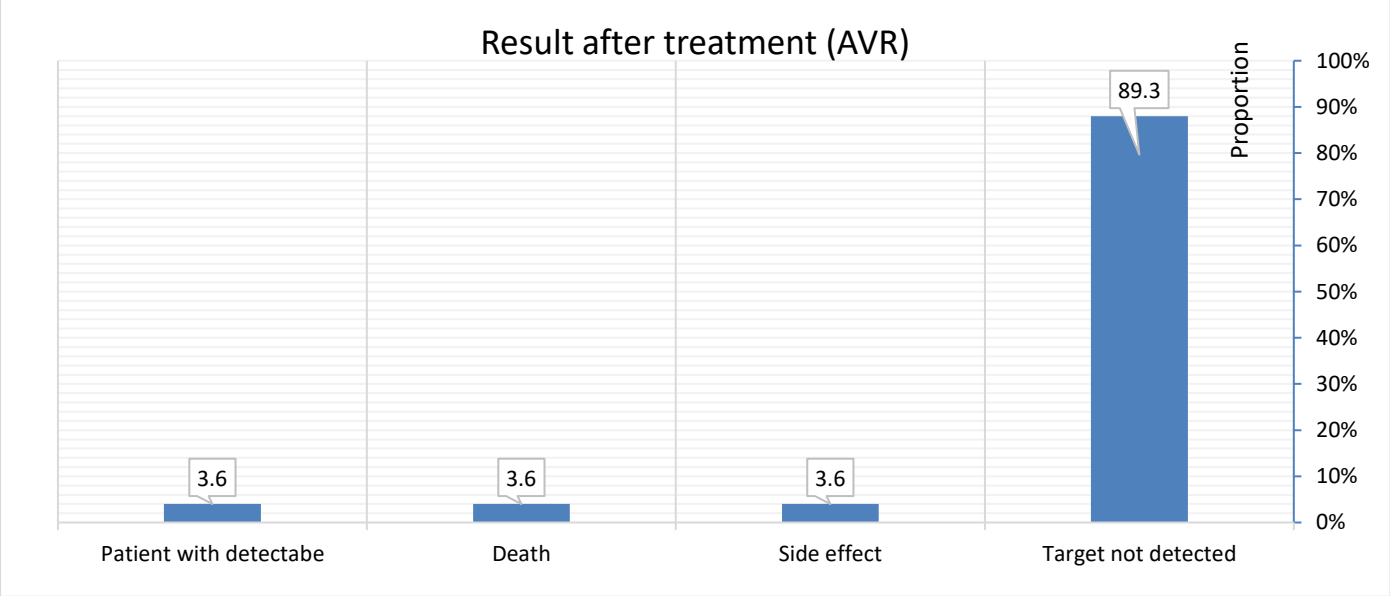

Figure 3. Early virological response (EVR)

3.3 Comparison of Pre- and Post-Treatment Virological Outcomes

All patients (100%) had detectable HCV RNA at baseline. Following treatment, 25 patients (89.3%) achieved undetectable viral levels, while 3 patients (10.7%) remained with detectable HCV RNA (Table 5).

This reduction in detectable HCV RNA following treatment was statistically significant (McNemar's test, $p < 0.001$), indicating a strong treatment effect.

3.4 Sustained Virological Response (SVR12)

Among the 25 patients who completed treatment and follow-up, all (100%; 95% CI: 86%–100%) achieved sustained virological response at 12 weeks post-treatment (SVR12), with no detectable HCV RNA (Table 6).

The treatment regimen was generally well tolerated. Only one patient (3.6%) discontinued therapy due to adverse effects, and one patient (3.6%) died during the study period. No additional serious adverse events were reported (Figure 4).

Overall, the combination of sofosbuvir and daclatasvir demonstrated high effectiveness in this cohort. A substantial proportion of patients achieved rapid viral clearance, as reflected by the high EVR rate, and all patients who completed treatment achieved SVR12. The statistically significant reduction in viral load further supports the efficacy of the regimen in this population.

Table 5. Comparison of HCV RNA status Pre- and Post-treatment

HCV RNA Status	Pre-treatment, n (%)	Post-treatment, n (%)
Detectable	28 (100)	3 (10.7)
Undetectable	0 (0)	25 (89.3)

Table 6. Sustained virological response (SVR12) (n = 25)

Outcome	n (%)
SVR12 (Undetectable HCV RNA)	25 (100)
Detectable HCV RNA	0 (0)

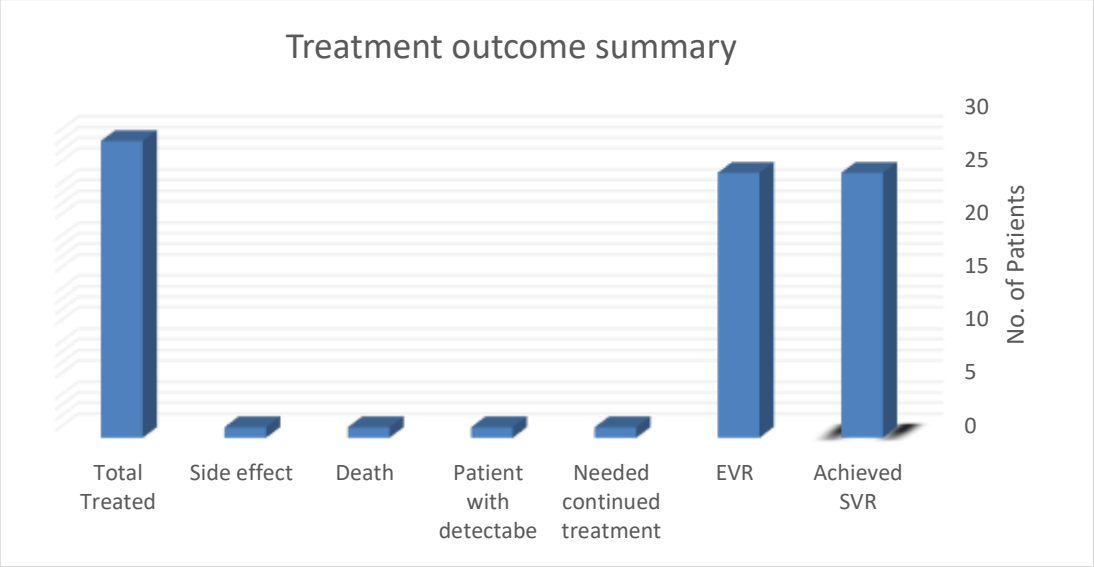

Figure 4. Treatment outcome summary

4. DISCUSSION

The present study evaluated the effectiveness and safety of a thrice-weekly regimen of sofosbuvir and daclatasvir in Yemeni patients with hepatitis C virus (HCV) infection undergoing maintenance hemodialysis. The findings demonstrate a high level of therapeutic efficacy, with an early virological response (EVR) rate of 89.3% and a sustained virological response at 12 weeks post-treatment (SVR12) of 100% among patients who completed therapy. These results provide important evidence supporting the feasibility of modified dosing strategies in resource-limited settings.

Patients undergoing hemodialysis represent a high-risk population for HCV infection due to repeated vascular access, exposure to blood products, and potential nosocomial transmission. The burden of HCV in this population remains substantial, particularly in low- and middle-income countries, where infection control practices and access to direct-acting antivirals (DAAs) may be suboptimal.[2] In this context, the identification of effective and accessible treatment regimens is of considerable clinical and public health importance.

The high SVR12 rate observed in this study is consistent with accumulating evidence demonstrating the efficacy of sofosbuvir-based regimens in patients with renal impairment. A systematic review and meta-analysis by Li et al. reported pooled SVR rates exceeding 95% in patients with advanced chronic kidney disease treated with sofosbuvir-containing regimens, supporting their effectiveness even in this traditionally difficult-to-treat population.[11] Similarly, Poustchi et al. demonstrated a 100% SVR rate in patients with severe renal impairment treated with sofosbuvir and daclatasvir, findings that closely align with those of the present study.[12]

However, variability in SVR outcomes has been reported across studies. Cheema et al. observed a lower SVR rate of 80.6% in hemodialysis patients treated with sofosbuvir and daclatasvir, which contrasts with the complete response observed in our cohort.[3] This discrepancy may be explained by differences in patient characteristics, including the presence of liver cirrhosis, baseline viral load, comorbidities, and treatment adherence. Advanced liver disease and resistance-associated substitutions (RASs), particularly within the NS5A region, have been identified as key factors associated with reduced treatment response.[13]

A notable aspect of the present study is the use of a reduced-frequency dosing regimen, with both sofosbuvir and daclatasvir administered three times weekly. Despite this modification, a 100% SVR12 rate was achieved among patients who completed therapy. This finding has important pharmacological implications. Sofosbuvir is primarily eliminated through renal excretion, and its inactive metabolite (GS-331007) accumulates in patients with impaired renal function. However, studies have shown that this metabolite is effectively cleared during hemodialysis, thereby reducing the risk of toxicity while maintaining adequate exposure to the active drug.[14] In contrast, daclatasvir undergoes hepatic metabolism and is minimally affected by renal impairment, allowing for consistent inhibition of the NS5A protein regardless of dialysis status.[10] The complementary mechanisms of action of these agents likely contribute to sustained viral suppression even with reduced dosing frequency.

From a safety perspective, the regimen was well tolerated, with only one patient discontinuing treatment due to adverse effects and no major drug-related complications reported. These findings are consistent with previous studies demonstrating the favorable safety profile of sofosbuvir- and daclatasvir-based regimens in patients with end-stage renal disease.[3,12] The low incidence of adverse events further supports the suitability of this regimen for use in vulnerable patient populations.

The clinical implications of these findings are particularly relevant for resource-limited settings such as Yemen, where access to guideline-recommended DAAs, such as glecaprevir/pibrentasvir or grazoprevir/elbasvir, may be restricted due to cost or availability. In such contexts, the use of alternative regimens based on locally available medications may provide a practical solution to expand treatment access. The results of this study suggest that a thrice-weekly regimen of sofosbuvir and daclatasvir may represent an effective and safe alternative in this setting.

Despite the promising results, several limitations should be acknowledged. The relatively small sample size limits the statistical power and generalizability of the findings. In addition, the single-center design may introduce selection bias, and the absence of a control group precludes direct comparison with other treatment regimens. Furthermore, a detailed assessment of liver disease severity and resistance-associated mutations was not performed, which may have provided additional insights into factors influencing treatment response.

5. CONCLUSION

The findings of this study demonstrate that a thrice-weekly regimen of sofosbuvir and daclatasvir is highly effective and well tolerated in patients with HCV infection undergoing maintenance hemodialysis. All patients who completed treatment achieved sustained virological response, indicating complete viral clearance despite the use of a reduced dosing frequency. These results suggest that modified dosing strategies may provide a viable and pragmatic alternative in resource-limited settings where access to guideline-recommended direct-acting antiviral regimens is restricted. The favorable safety profile observed further supports the clinical applicability of this approach in patients with advanced renal impairment. However, the relatively small sample size and single-center design warrant cautious interpretation of the findings. Larger, multicenter studies with longer follow-up durations are needed to confirm these results and to further define optimal dosing strategies for this high-risk population.

Ethical Approval

Ethical approval for the study was granted by the Ethical Committee of the Faculty of Medicine, Taiz University, Taiz, Yemen.

Acknowledgement

All praise and thanks are due to Allah for His grace and guidance in completing this work. We sincerely thank Dr. Amal Al-Hakimi for valuable support and guidance throughout this study. We also express our heartfelt gratitude to our family members for their continuous support and encouragement.

Competing Interests

All the authors declare that there are no conflicts of interest.

Funding Information

No funds were received for this study.

Underlying Data

Derived data supporting the findings of this study are available from the corresponding author on request.

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