



Efficacy of Sofosbuvir and Velpatasvir in Achieving Sustained Virological Response in Patients with End- Stage Renal Disease Infected with Hepatitis C Virus

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ABSTRACT

Background: Hepatitis C virus (HCV) infection remains a critical concern globally, especially in populations with end-stage renal disease (ESRD) on haemodialysis. This study aims to evaluate the efficacy and safety of a fixed-dose combination of Sofosbuvir and Velpatasvir (SOF/VEL) in achieving sustained virological response at 12 weeks post-treatment (SVR12) among ESRD patients infected with genotype III HCV

Methods: A prospective cohort study was conducted at the Sindh Institute of Urology and Transplantation, Karachi, from January 2023 to December 2024. Inclusion criteria were patients aged ≥ 18 years with ESRD on maintenance hemodialysis for ≥ 3 months and genotype III HCV infection. Patients received SOF/VEL (400 mg/100 mg) daily with ribavirin (400 mg) once weekly for 12 weeks. Primary outcome measured was SVR12. Statistical analyses involved Chi-square and Student's t-tests, with significance set at $p < 0.05$.

Results: Of 109 enrolled patients (mean age 30.45 ± 8.98 years; 75.2% male), 105 (96.3%) achieved an end-of-treatment response (ETR), while SVR12 was attained in 91 (84.3%) patients. The mean duration of dialysis was 3.1 ± 1.2 years. The most common adverse effects were fatigue (28%), headache (18%), and nausea (12%). Significant biochemical improvements at treatment completion were noted in ALT ($p=0.001$) and AST ($p=0.021$), although biochemical changes were not significantly correlated with SVR12.

Conclusion: The combination therapy of Sofosbuvir and Velpatasvir demonstrated good efficacy (84.3% SVR12) and a manageable safety profile in ESRD patients on hemodialysis infected with HCV genotype III. Further multi-center studies with larger sample sizes are necessary to validate and generalize these results, emphasizing the potential of SOF/VEL therapy in this challenging patient population.

Keywords: End-stage renal disease; Hepatitis C; genotype III; ETR; SVR.

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INTRODUCTION

Intestinal obstruction is one of the most frequent surgical emergency conditions globally, defined by the impairment of regular intestinal movement caused by mechanical or functional factors.¹ It has clinical manifestations of abdominal pain, distension, vomiting, and constipation and may lead to severe life-threatening complications requiring prompt diagnosis and management to prevent serious complications.² Intestinal obstruction due to postoperative adhesions is the most common cause, but the virgin abdomen poses a diagnostic and therapeutic challenge. These cases do not have the adhesions which may be used as a diagnostic clue therefore raise suspicions of other possible causes.³

Therefore, the etiology of intestinal obstruction globally can be described as varying with respect to geographic and demographic factors.⁴ Various studies in high income countries show that malignancies and hernias are most frequent causes of emergency abdominal surgery while in low and middle income countries hernias, volvulus, and infection are most frequent.^{1,5} However, a search for primary causes and outcomes of obstruction in patients with virgin abdomen was not conducted due to the scarcity of corresponding research in Pakistan. Understanding these factors is essential for improving clinical outcomes and reducing complications.

Patients presenting with a virgin abdomen may have hernias, tumours, volvulus, intussusception or other functional obstructions like paralytic ileus.^{6,7} These etiologies need individual approaches in terms of management and may range from medical management to emergent surgical intervention. However, the available data regarding the incidence and outcomes related to these patients in Pakistan are quite scarce and thus, it becomes challenging for the healthcare workers involved to adhere to guidelines for managing this specific patient population.

The rationale for this study lies in addressing this critical gap in knowledge. This research seeks to explore the etiological spectrum, clinical presentations, and prognosis of intestinal obstruction in adults with virgin abdomens to provide a deeper understanding of this condition in a local context. The findings can help guide early diagnosis, improve management protocols, and ultimately enhance patient care. The primary objective of this study was to identify the causes, clinical features, and outcomes of intestinal obstruction in adults with a virgin abdomen at Lady Reading Hospital, Peshawar. This research seeks evidence-based data to support effective decision-making and improve patient outcomes.

METHODS

After the approval from the ethical review committee (**Ref # SIUT-ERC-2022/A-729**), Sindh Institute of Urology and Transplantation, this prospective cohort study was carried out at the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan, from 1st January 2023 to 31st December 2024. This study included all the patients with ESRD aged ≥ 18 years on maintenance hemodialysis for ≥ 3 months and having HCV infection (genotype III). HCV infection was defined as detectable HCV RNA PCR. This study excluded patients having coinfection of HCV with either HBV or HIV; patients with decompensated liver disease (Child-Pugh Class C); previous history of treatment with direct acting antivirals (DAAs); pregnant or lactating mothers; those with any active malignancy and those who were lost to follow up during the course of treatment. Based on previous studies reporting SVR12 rates of $\sim 95\%$ with SOF/VEL in ESRD patients, a minimum sample of 109 patients was estimated using a confidence level of 95% and a margin of error of 5%¹⁶. All eligible patients received a fixed-dose combination of sofosbuvir (400 mg) and velpatasvir (100 mg) once daily for 12 weeks with ribavirin 400mg once weekly for 12 weeks. After the informed consent, all the baseline characteristics including the demographic data, duration of hemodialysis, laboratory parameters including complete blood count, liver function tests were recorded. HCV RNA levels were measured at baseline end of treatment (EOT) and sustained virological response at 12 weeks (SVR12). The safety profile and side effects of the medication were also noted.

Statistical analysis was performed using SPSS version 25. Continuous variables were expressed as mean \pm SD, and categorical variables as frequencies and percentages. The primary endpoint was SVR12. Comparative analysis was performed using the Chi-square test for categorical variables while that for continuous variables was done using the student t-test. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 109)

Variable	Value
Age (years), mean \pm SD	30.45 \pm 8.98
Male sex, n (%)	82 (75.2)
Female sex, n (%)	27 (24.8)
Duration of hemodialysis (years), mean \pm SD	3.1 \pm 1.2

A total of 109 patients with end-stage renal disease on maintenance hemodialysis infected with hepatitis C infection were enrolled in the study. Mean age was 30.45 ± 8.98 years. Among the studied population, 82 (75.2%) were males; while 27 (24.8%) were females.

Table 2. Baseline Laboratory Parameters of the Study Population (n = 109)

Laboratory Parameter	Mean \pm SD
Hemoglobin (g/dL)	9.97 ± 1.87
Total leukocyte count ($\times 10^9/L$)	6.9 ± 2.3
Platelet count ($\times 10^9/L$)	206 ± 83
Total bilirubin (mg/dL)	0.6 ± 0.22
Alanine aminotransferase (ALT) (IU/L)	27.9 ± 31.3
Aspartate aminotransferase (AST) (IU/L)	30.1 ± 23.7
Serum albumin (g/dL)	3.9 ± 0.6

Mean duration of hemodialysis: 3.1 ± 1.2 years. Mean hemoglobin was 9.97 ± 1.87 g/dl, TLC was $6.9 \pm 2.3 \times 10^9/L$, platelet was $206 \pm 83 \times 10^9/L$, total bilirubin was 0.6 ± 0.22 mg/dl, ALT was 27.9 ± 31.3 IU/L and AST was 30.1 ± 23.7 IU/L and serum albumin was 3.9 ± 0.6 g/dl.

Table 3. Treatment Response Outcomes

Treatment Outcome	n (%)
End of Treatment Response (ETR)	105 (96.3)
Sustained Virological Response at 12 weeks (SVR12)	91 (84.3)
Adverse Effect	
Fatigue	28 (28.0)
Headache	18 (18.0)
Nausea	12 (12.0)

An End of Treatment Response (ETR) was achieved in 105 (96.3%) patients, while a sustained virological response at 12 weeks (SVR12) was achieved in 91 (84.3%) patients. The most common side effect observed in the treated population was fatigue in 28% followed by headache and nausea in (18%) and (12%) patients respectively.

On comparative analysis, ALT ($p \leq 0.001$) and AST ($p=0.021$) were significantly lower in patients

achieving ETR. However, no significant improvement in laboratory parameters was observed in patients achieving SVR12.

DISCUSSION

This study evaluated the efficacy of Sofosbuvir and Velpatasvir (SOF/VEL) in achieving sustained virological response (SVR12) in hepatitis C virus (HCV)-infected end-stage renal disease (ESRD) maintenance hemodialysis patients. Our study yielded an SVR12 rate of 84.3%, making SOF/VEL an effective therapeutic regimen in this challenging population.

Comparing our results with the literature, Liu et al. observed higher SVR12 rates of 94.8% and 100% by evaluable population (EP) and per-protocol (PP) analyses, respectively, in patients with stages 4 or 5 of chronic kidney disease (CKD). In this multi-center Taiwanese study involving patients with liver diseases that were either compensated or decompensated, the results show excellent effectiveness and tolerability even in the most severe renal impairment¹⁶. The relatively lower SVR12 rate observed in our study could be due to regional differences, differences in the baseline characteristics of the patient population, dialysis practices, and the fact that we included the patients infected with the genotype III HCV, which is considered a difficult genotype in-terms of HCV management. Similarly, studies reported SVR12 rates of about 95% in the case of ESRD patients and emphasized SOF/VEL's robust antiviral activity in this group^{17,18,19}

The adverse events reported in the literature included fatigue, headache, nausea, insomnia, and pruritus^{16,17}. Side effects tended to be mild to moderate and manageable, and paralleled our findings of fatigue (28%), headache (18%), and nausea (12%) being the most common adverse events. These pooled results further support the manageable safety profile of SOF/VEL therapy for the patient population with ESRD.

Furthermore, Literature proposed significant reductions in liver enzymes (AST and ALT) at the end of treatment (ETR) in ESRD patients with HCV infection undergoing treatment with direct-acting antiviral therapy^{16,20,21}. In our study, we observed significant improvement in liver enzymes at end of the treatment. However, biochemical response correlating with SVR12 achievement was not consistently observed in the current study, suggesting virological and biochemical interaction complexity after treatment. One difference in our approach was the routine use of low-dose ribavirin, in contrast to the previous evaluation of SOF/VEL with and without ribavirin. It was reported that comparable SVR12 rates regardless of ribavirin use, suggesting that ribavirin may not have a substantial improvement on outcomes but potentially add adverse effects^{16,22,23}.

Certain limitations can be attributed to our study. At first, single centered design and secondly, the small sample size of this study may limit the generalizability of the results, and multicentered studies with large sample sizes are required to validate the results of this study.

Overall, our study, also corroborated by literature, unveils the safety and efficacy of SOF/VEL as a commendable therapeutic option for HCV-infected ESRD hemodialysis patients^{24,25}. In consideration of the pronounced prevalence of HCV globally in dialysis populations, our outcome strongly favors the clinical application of SOF/VEL regimens for the improvement of patient outcomes and the quality of care.

CONCLUSION:

This study showed that Sofosbuvir and Velpatasvir-based combination therapy is a commendable treatment option for patients with ESRD infected with hepatitis C and is associated with improvement in patients' outcomes and quality of life and care in this population. However, multicenter studies with large sample sizes are required to validate our results.

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CONFLICT OF INTEREST

None

ETHICAL APPROVAL

This study was approved by SIUT-Ethical Review Committee (SIUT-ERC) (Approval No: SIUT-ERC-2022/A-729, dated October 7, 2022).

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE guidelines

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