Open Access

Original Article

Efficacy of Sofosbuvir/Velpatasvir (SOF/VEL) Combination in Children with Chronic Hepatitis C: A Prospective Study

Samina Khan, Farooq Ikram, Saadiya Mushtaq*, Husna Khan, Ifnan Shamraiz, Adnan Shahzad*

Department of Paediatric Gastroenterology and Hepatology, Combined Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan, *Department of Virology, Armed Forces Institute of Pathology, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To evaluate the efficacy and safety of Sofosbuvir/Velpatasvir (SOF/VEL) combination therapy in children aged 3–12 years with chronic hepatitis C (CHC).

Study Design: Prospective analytical study.

Place and Duration of Study: Department of Paediatric Gastroenterology and Hepatology, Combined Military Hospital, Rawalpindi, Pakistan, from Oct 2023 to Dec 2024.

Methodology: Fifty-eight treatment-naive children (3–12 years) with confirmed CHC infection and normal baseline liver ultrasound were enrolled using non-probability consecutive sampling. Patients with cirrhosis, hepatitis B surface antigen (HBsAg) positivity, or impaired renal function were excluded. All participants received a weight-based fixed dose of Sofosbuvir and Velpatasvir. Treatment response was assessed by hepatitis C virus ribonucleic acid polymerase chain reaction (HCV RNA PCR) at baseline, at the end of treatment (end-of-treatment response), and 12 weeks after completion of therapy (sustained virological response at 12 weeks [SVR12]). Adverse events were monitored prospectively. Data were analysed using R statistical software, and a p-value < 0.05 was considered statistically significant.

Results: The mean age was 7.2±2.5 years, with 53.5% female participants. Genotype 3 was predominant (72.4%). Most individuals had no comorbidities (58.6%), although thalassemia major was relatively frequent (24.1%). Overall, an SVR12 rate of 94.8% (n=55) was achieved. Mean HCV RNA levels declined from 3.39 million IU/mL to 400 IU/mL (p<0.001). Side effects were mostly mild; 62.1% reported none.

Conclusion: Sofosbuvir/Velpatasvir demonstrated excellent efficacy and tolerability in children with CHC, supporting its role as a first-line therapy in paediatric populations.

Keywords: Antiviral Agents, Child, Chronic Hepatitis C, Pakistan, Sofosbuvir, Velpatasvir.

How to Cite This Article: *Khan S, Ikram F, Mushtaq S, Khan H, Shamraiz I, Shahzad A. Efficacy of Sofosbuvir/Velpatasvir (SOF/VEL) Combination in Children with chronic Hepatitis C: A Prospective Study. Pak Armed Forces Med J 2026; 76(Suppl-8): S1277-S1281.*
DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-8.13864

INTRODUCTION

Hepatitis C is considered by the World Health Organisation (WHO) to be a major global public health challenge.[1] Pakistan has the second-highest prevalence of this disease after China.[2] In children, the estimated seroprevalence is 1.6%, with genotype 3 being the most common strain.[3] Vertical transmission is the primary route of infection in this age group.[4] Around one in five children can clear the virus spontaneously within the first four years of life, while the majority develop chronic infection.[5]

In chronic hepatitis C, cirrhosis occurs in only 1%–4% of cases, leading to the perception of a mild disease. However, recent ESPGHAN guidelines recommend treatment from age 3 years to prevent long-term complications. The advent of oral direct-acting antivirals (DAAs) has made this approach feasible, offering safer and more effective therapy than interferon-based regimens.[6] Pediatric studies report sustained virologic response rates of 98%–100% across various direct-acting antiviral combinations and HCV genotypes.[7]

Sofosbuvir/Velpatasvir (SOF/VEL) is a fixed-dose combination of two direct-acting antivirals. Sofosbuvir inhibits the hepatitis C virus (HCV) NS5B RNA-dependent RNA polymerase, while Velpatasvir targets the NS5A protein involved in viral replication and assembly. Based on results from a small industry-sponsored trial, SOF/VEL has been approved for paediatric use in children aged 3 years and older since 2022.[8]

This study aimed to determine the efficacy of Sofosbuvir/Velpatasvir combination therapy in children with chronic hepatitis C HCV infection, aged 3-12 years in our setup, as evaluating this therapy in younger patients is essential for early intervention and prevention of long-term liver complications.

Correspondence: Dr Samina Khan, Department of Paediatric Gastroenterology, Combined Military Hospital, Rawalpindi Pakistan
Received: 19 Sep 2025; revision received: 18 Dec 2025; accepted: 19 Dec 2025

METHODOLOGY

This prospective analytical study was conducted at the Paediatric Gastroenterology and Hepatology Department of the Combined Military Hospital (CMH) in Rawalpindi, Pakistan, from October 2023 to December 2024. The study was approved by the Institutional Ethical Review Committee (IRB Serial No. 472 dated 26/10/2023).

Inclusion Criteria: Children of either gender, aged 3 to 12 years with a confirmed diagnosis of chronic hepatitis C which was defined as the persistence of detectable hepatitis C virus (HCV) RNA in the blood for more than six months, those with a normal renal profile, and those who were treatment-naïve, meaning those who had never received any form of antiviral therapy for HCV, were included.

Exclusion Criteria: Patients positive for hepatitis B surface antigen (HbsAg), and those with findings of cirrhosis on ultrasound, were excluded.

A sample size was of 58 participants was calculated using OpenEpi software based on a previously reported 92% efficacy of the Sofosbuvir/Velpatasvir combination in children with chronic hepatitis C.[9] Written informed consent was obtained from the parents or legal guardians of every child before inclusion in the study, and data was collected using a non-probability consecutive sampling.

A total of 62 children were screened for eligibility; four were excluded due to associated HBsAg positivity or cirrhosis, leaving a final enrolled cohort of 58 patients. The enrollment process, treatment administration, and participant disposition throughout the study are detailed in the patient flow diagram Figure.

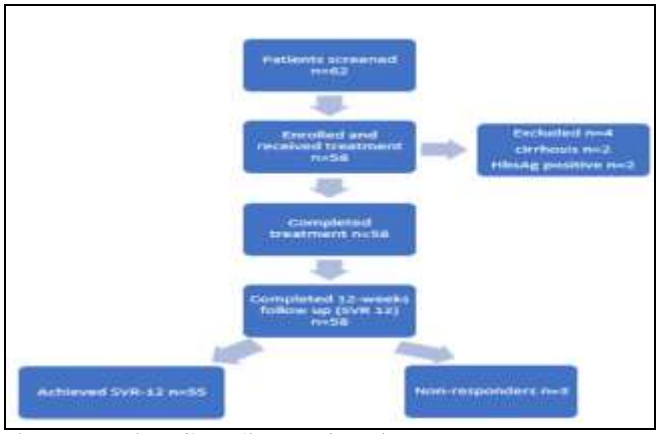

Figure-1; Patient flow diagram (n=58)

The diagnosis of hepatitis C virus (HCV) infection was established by detecting HCV RNA using reverse transcription-polymerase chain reaction (RT-PCR). Liver status was evaluated through liver function tests and imaging studies. An abdominal ultrasound was performed at the initial visit.

For each patient, baseline demographic and clinical data were collected, including age in years, gender, and weight in kilograms. Clinical details collected included the primary diagnosis or comorbid conditions (congenital, hematological, or oncological disorders). Risk factors such as family history of HCV infection, history of blood transfusions, and past surgical procedures were also recorded. Baseline HCV genotype testing was performed to determine viral subtypes.

All patients received a fixed-dose combination of velpatasvir (100 mg) and sofosbuvir (400 mg), prescribed according to body weight. Treatment response was monitored by measuring HCV PCR and serum alanine aminotransferase (ALT) at baseline, at the end of treatment (ETR), and again 12 weeks after treatment completion to assess sustained virological response (SVR12). RT-PCR at SVR12 was considered the primary measure of efficacy. Adverse events were monitored prospectively through phone calls and during monthly follow-up visits. Guardians and children who could communicate were asked about side effects, including nausea, vomiting, abdominal pain, diarrhea, fever, headache, lethargy, insomnia, or any other new symptoms.

Data analysis was performed using R software version 4.3.3. Numerical variables were presented as Mean±SD, or as median with inter-quartile range (IQR) in the case of skewed distributions, while categorical variables were expressed as frequencies and percentages. Outcome measures (RT-PCR results and ALT levels) were analyzed using Kruskal Wallis to compares changes in HCV PCR and ALT over three times, and Fisher exact test to compare treatment efficacy according to different patient characteristics were applied to compare pre- and post-treatment values. A p-value of <0.05 was considered statistically significant.

RESULTS

The total number of participants was 58. Their mean age was 7.2±2.5 years, and mean weight was 21.7±7.1 kg. There were 31(53.5%) females, and most (n=38, 65.5%) were in the 3-to-8-year age group (Table-I).

Table-I: Demographic Characteristics of Children with Chronic Hepatitis C (n=58)

Demographics	Values
Age in years (Mean±SD)	7.22 ± 2.52
Weight in kilograms (Mean±SD)	21.67 ± 7.12
Gender	
Female	31 (53.45)
Male	27 (46.55)
Age groups in years	
3-8	38 (65.52)
9-12	20 (34.48)

The most frequent co-diagnosis was thalassemia major (n=14, 24.1%), followed by cerebral palsy (n=4, 6.9%), Down syndrome with AML (n=3, 5.2%), and hepatoblastoma (n=3, 5.2%), more than half had no associated condition (n=34, 58.6%). A positive family history was reported in (n=10, 17.1%) of the study participants. Almost half had received blood transfusions (n=27, 46.6%). A surgical history was present in (n=17, 29.3%) patients. HCV genotype 3 was predominant (n=42, 72.4%), while genotype 1 was found in (n=3, 5.2%), and genotype was not available for (n=13, 22.4%) children (Table-II).

Table-II: Baseline Clinical Characteristics and Histories of Study Participants (n=58)

Characteristic	n (%)
Diagnosis	
Cerebral palsy	4(6.90)
Down Syndrome with AML	3(5.17)
Hepatoblastoma	3(5.17)
No comorbid condition	34(58.62)
Thalassemia Major	14(24.14)
Family History	
No	48(82.75)
Yes	10(17.25)
Blood transfusion	
No	31(53.45)
Yes	27(46.55)
Surgical history	
No	41(70.69)
Yes	17(29.31)

Most children reported no side effects (n=36, 62.1%). The most common adverse event was abdominal pain (n=7, 12.1%), followed by anorexia (n=4, 6.9%), vomiting (n=4, 6.9%), anorexia with headache and vomiting (n=4, 6.9%), and anorexia with loose motions and fever (n=3, 5.2%).

Both viral load (PCR) and ALT levels showed a significant decline over time. Median HCV PCR levels dropped sharply from 489,853.5 IU/mL (IQR: 110,801–1,066,650.75) at baseline to 0 IU/mL at both the end of treatment and the 3-month follow-up, indicating complete viral suppression in most patients. Median ALT levels also decreased markedly, falling from 66.5 U/L (IQR: 36.25–100.25) at baseline to 23 U/L (IQR: 19–31) at the end of treatment and further to 21 U/L (IQR: 18–27) at 3 months. Both reductions were statistically significant (p<0.001), reflecting strong biochemical and virological response to therapy. Values calculated using Kruskal-Wallis test can be seen in Table-III.

Table-III: Changes in Hepatitis C Virus (HCV) Polymerase Chain Reaction (PCR) and Alanine Aminotransferase (ALT) over time in children with Chronic Hepatitis C (n=58)

Parameters	Study group			*p*-value
	Initial treatment (n=58) Median (IQR)	At 3 Months (n=58) Median (IQR)	End of Treatment (n=58) Median (IQR)	
PCR	489853.50 (110801.00-1066650.75)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	<0.001
ALT	66.5 (36.25-100.25)	21.00 (18.00-27.00)	23.00 (19.00-31.00)	<0.001

Treatment with Sofosbuvir/Velpatasvir was effective in 55 children (94.8%), with only 3(5.2%) showing no response. Efficacy did not differ significantly by age group (p=0.54), gender (p=0.09), family history (p=1.00), blood transfusion history (p=0.59), surgical history (p=0.65), or HCV genotype (p=0.16). Although genotype 1 had a numerically lower response (n=2; 66.7%), this difference was not statistically significant (Table-IV).

Table-IV: Treatment Efficacy according to different Patient Characteristics (n=58)

Characteristic	Effective	Not effective	*p*-value
Age group n(%) n(%)			0.54
3–8 years	35 (92.1)	3 (7.9)	
9–12 years	20 (100.0)	0 (0.0)	
Gender			0.09
Female	31 (100.0)	0 (0.0)	
Male	24 (88.9)	3 (11.1)	
Family history			1.00
No	45 (93.8)	3 (6.3)	
Yes	10 (100.0)	0 (0.0)	
Blood transfusion			0.59
No	30 (96.8)	1 (3.2)	
Yes	25 (92.6)	2 (7.4)	
Surgical history			0.65
No	39 (95.1)	2 (4.9)	
Dental procedure	3 (100.0)	0 (0.0)	
Post trauma, stitches	3 (100.0)	0 (0.0)	
Surgical procedure	10 (90.9)	1 (9.1)	
HCV genotype			0.16
1	2 (66.7)	1 (33.3)	
3	40 (95.2)	2 (4.8)	
Not tested	13 (100.0)	0 (0.0)	

**HCV: Hepatitis C Virus*

DISCUSSION

In this cohort of 58 children with chronic hepatitis C, treatment with Sofosbuvir/Velpatasvir (SOF/VEL) demonstrated excellent efficacy, with 94.8% achieving sustained virological response. The mean viral load dropped markedly from 3.4 million IU/mL at baseline to 228 IU/mL at the end of treatment and remained suppressed at the three-month follow-up (p<0.001). Liver enzyme levels also showed significant improvement, as alanine aminotransferase decreased from an average of 102 U/L before therapy to 29 U/L at treatment completion and further to 24 U/L at follow-up (p<0.001).

In a multicenter trial involving 216 paediatric patients aged 3 to 18 years, once-daily treatment with Sofosbuvir/Velpatasvir (SOF/VEL) for 12 weeks resulted in an overall sustained virological response at 12 weeks (SVR12) of about 92% across all genotypes. The regimen was generally well tolerated, with no unexpected safety concerns reported.[11] Our slightly lower response rate may reflect differences in baseline viral load or adherence patterns, which are typical in younger age groups. In a paediatric study conducted, children aged 3 to 17 years received Sofosbuvir/Velpatasvir for 12 weeks, achieving an SVR12 of 92.7% (38 out of 41). Treatment was associated with significant biochemical and clinical improvement, while adverse events were mostly mild in nature.[12] The similar biochemical improvements observed in our study further support its hepatoprotective role. In the PANDAA-PED real-world clinical trial, 50 children aged 6 to 18 years were treated with Sofosbuvir/Velpatasvir for 12 weeks, and all achieved SVR12, reflecting a 100% response rate. The treatment was well tolerated, with only mild to moderate adverse events reported.[13]

The high rate of sustained virological response observed aligns with the pan-genotypic activity of Sofosbuvir/Velpatasvir, which targets both the NS5B RNA polymerase and the NS5A protein essential for viral replication. However, treatment outcomes did not vary significantly across genotypes, sex, age, transfusion history, or surgical history. Although a numerically lower response was seen in children with genotype 1 (66.7%), this difference was not statistically significant, most likely owing to the small number of patients in this subgroup. One study reported pooled SVR12/24 rates of approximately 94% for genotype 3, reinforcing the robustness of our findings in regions where this genotype is most prevalent.[14] These results confirm that SOF/VEL is a highly effective therapeutic option for children across diverse populations.

In the adult setting, the landmark ASTRAL-2 and ASTRAL-3 trials demonstrated that a 12-week course of Sofosbuvir/Velpatasvir achieved SVR12 rates of 99% in genotype 2 and 95% in genotype 3, outcomes that were clearly superior to sofosbuvir combined with ribavirin. These findings established the pan-genotypic efficacy of SOF/VEL and provided the foundation for its subsequent evaluation and development in paediatric populations.[15]

In our cohort, SOF/VEL was well tolerated, with 62.1% of children experiencing no adverse events, while the events that did occur were generally mild and self-limiting, including abdominal pain, anorexia, vomiting, and transient fever. No child required treatment discontinuation due to drug-related toxicity.[15] Consistent with findings from Foster *et al.*, our results support the high efficacy and favourable safety profile of sofosbuvir/velpatasvir in pediatric HCV, reinforcing its role as a pan-genotypic, well-tolerated regime.[16] In a large multicenter clinical trial involving children aged 3 to 17 years, the frequency of serious adverse events was similarly low, with headache, fatigue, and gastrointestinal symptoms such as nausea and vomiting being the most frequently reported treatment-emergent events.[11] Importantly, only three cases of virological failure were observed, and none of the participants discontinued therapy due to adverse effects attributable to the drug.

The predominance of genotype 3 in this cohort highlights the critical role of pan-genotypic regimens in the South Asian context. The approval of SOF/VEL by the FDA in 2020 for children aged six years and above marked a significant milestone in paediatric HCV management.[17] Integrating SOF/VEL into national treatment programs has the potential to substantially accelerate progress towards the WHO goal of hepatitis C elimination by 2030, particularly in high-burden countries such as Pakistan.[18]

LIMITATIONS OF STUDY

The study has several limitations, including the absence of a control group, a short three-month post-treatment follow-up, and incomplete genotyping in about 22% of participants. Moreover, the small number of genotype 1 cases limits the generalizability of the findings. A longer follow-up is warranted to confirm the durability of viral suppression and assess long-term effects on growth and liver fibrosis progression.

CONCLUSION

We found that sofosbuvir/velpatasvir can be a highly effective and well-tolerated treatment for children with chronic hepatitis C, achieving high cure rates regardless of demographic or clinical factors.

Conflict of Interest: None.

Discolure:

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SK & FI: Data acquisition, data analysis, critical review, approval of the final version to be published.

SM & HK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

IS & AS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFRENCES

1. Brunner N, Bruggmann P. Trends of the global hepatitis C disease burden: Strategies to achieve elimination. J Prev Med Public Health 2021; 54(4): 251–258. https://doi.org/10.3961/jpmph.21.151
2. Saleem U, Aslam N, Siddique R, Iqbal S, Manan M. Hepatitis C virus: Its prevalence, risk factors and genotype distribution in Pakistan. Eur J Inflamm 2022; 20: 1721727X221144391. https://doi.org/10.1177/1721727X221144391
3. Guntipalli P, Pakala R, Kumari GS, Ahmed F, Bhatnagar A, Endaya CMK, et al. Worldwide prevalence, genotype distribution and management of hepatitis C. Acta Gastroenterol Belg 2021; 84(4): 633–652. https://doi.org/10.51821/84.4.015
4. Ades AE, Gordon F, Scott K, Collins IJ, Claire T, Pembrey L, et al. Overall vertical transmission of hepatitis C virus, transmission net of clearance, and timing of transmission. Clin Infect Dis 2022; 76(5): 905–912. https://doi.org/10.1093/cid/ciac270
5. Musto F, Stracuzzi M, Crivellaro E, Rubinacci V, Cibarelli A, Porro C, et al. Natural history and management of hepatitis C in children: 25 years experience of a reference center in Northern Italy. Pediatr Infect Dis J 2024; 43(9): 813–818. https://doi.org/10.1097/inf.0000000000004374
6. Sintusek P, Phewplung T, Sanpavat A, Poovorawan Y. Liver tumors in children with chronic liver diseases. World J Gastrointest Oncol 2021; 13(11): 1680–1695. https://doi.org/10.4251/wjgo.v13.i11.1680
7. Indolfi G, Gonzalez-Peralta RP, Jonas MM, Sayed MH, Fischler B, Sokal E, et al. Espghan recommendations on treatment of chronic hepatitis C virus infection in adolescents and children including those living in resource-limited settings. J Pediatr Gastroenterol Nutr 2024; 78(4): 957–972. https://doi.org/10.1002/jpn3.12160
8. Di Marco L, Cannova S, Ferrigno E, Landro G, Nonni R, Mantia CL, et al. A comprehensive review of antiviral therapy for hepatitis C: The long journey from Interferon to pan-genotypic direct-acting antivirals (Daas). Viruses 2025; 17(2): 163-175. https://doi.org/10.3390/v17020163
9. Indolfi G, Easterbrook P, Giometto S, Malik F, Chou R, Lucenteforte E. Efficacy and safety of daa in children and adolescents with chronic hcv infection: A systematic review and meta-analysis. Liver Int 2024; 44(3): 663–681. https://doi.org/10.1111/liv.15827
10. European Medicines Agency. Epclusa [Internet]. [cited 2023 Feb 8]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/epclusa
11. Jonas M, Romero R, Sokal E. Safety and efficacy of sofosbuvir/velpatasvir in pediatric patients 6 to <18 years old with chronic hepatitis C infection. Hepatology 2019; 70(Suppl1): 748. https://www.hcvguidelines.org/references/jonas-2019a
12. Jonas MM, Romero R, Rosenthal P, Lin C, Verucchi G, Wen J, et al. Sofosbuvir–velpatasvir in children 3–17 years old with hepatitis C virus infection. J Pediatr Gastroenterol Nutr 2024; 78(6): 1342–1354. https://doi.org/10.1002/jpn3.12045
13. Pokorska-Śpiewak M, Talarek E, Aniszewska M, Pluta M, Dobrzeniecka A, Marczyńska M, et al. Efficacy and safety of treatment with sofosbuvir/velpatasvir in patients aged 6–18 years with chronic hepatitis C—results of the pandaa-ped study. Liver Int 2023; 43(9): 1871–1878. https://doi.org/10.1111/liv.15637
14. Mahmud S, Hossain MDB, Haque E, Baidya M, Rashid R, Hasan AR, et al. Effectiveness and safety of sofosbuvir/velpatasvir in chronic hepatitis C virus infection of Bangladeshi children. Egypt Liver J 2025; 15(1). https://doi.org/10.1186/s43066-025-00430-2
15. Petruzziello A, Marigliano S, Loquercio G, Cozzolino A, Cacciapuoti C. Global epidemiology of hepatitis C virus infection: An up-date of the distribution and circulation of hepatitis C virus genotypes. World J Gastroenterol 2016;22(34):7824. https://doi.org/10.3748/wjg.v22.i34.7824
16. Foster GR, Afdhal N, Roberts SK, Bräu N, Gane EJ, Pianko S, et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. N Engl J Med 2015; 373(27): 2608–2617. https://doi.org/10.1056/nejmoa1512612
17. US Food and Drug Administration. FDA approves new treatment for pediatric patients with any strain of hepatitis C. Silver Spring (MD): FDA; 2020 [cited 2023 Feb 8]. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-pediatric-patients-any-strain-hepatitis-c
18. Mahmud S, Al Kanaani Z, Abu-Raddad LJ. Characterization of the hepatitis C virus epidemic in Pakistan. BMC Infect Dis 2019; 19(1). https://doi.org/10.1186/s12879-019-4403-7