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EFFICACY OF VITAMIN D SUPPLEMENTATION ALONG WITH STANDARD ANTI-VIRAL THERAPY IN PATIENTS OF CHRONIC HEPATITIS C

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Abstract

Background: *Chronic hepatitis C remains a major cause of liver-related morbidity worldwide. Despite high cure rates with direct-acting antiviral therapy, factors influencing sustained viral response continue to be explored.*

Objective: *To compare the frequency of sustained viral response of vitamin D supplementation versus control along with standard therapy in patients of chronic hepatitis C.*

Methods: *This non-randomized controlled trial was conducted at Medicine Department of Farooq Hospital Westwood Branch, Lahore/Akhtar Saeed Trust Teaching Hospital, Lahore. A total of 120 patients with chronic hepatitis C were enrolled and divided into two groups: a vitamin D supplementation group (n = 60) receiving standard antiviral therapy plus oral vitamin D, and a control group (n = 60) receiving antiviral therapy alone.*

Results: *Baseline characteristics were comparable between the two groups, including age (46.8 ± 11.2 vs 47.5 ± 10.9 years), body mass index (26.1 ± 3.4 vs 26.4 ± 3.6 kg/m²), and baseline serum vitamin D levels (17.2 ± 5.1 vs 18.0 ± 5.4 ng/ml). At 12 weeks, sustained viral response was achieved in 86.7% of patients in the vitamin D group compared to 76.7% in the control group. At 24 weeks, sustained viral response was significantly higher in the vitamin D group (83.3%) compared to the control group (68.3%) (p = 0.04). Improved response rates with vitamin D supplementation were observed across age groups, gender, comorbidity status, and Child-Pugh class A liver disease.*

Conclusion: *Vitamin D supplementation as an adjunct to standard antiviral therapy significantly improves sustained viral response in patients with chronic hepatitis C without compromising treatment adherence or safety.*

Introduction

Chronic hepatitis C virus (HCV) infection has been a significant population health issue of global concern, with millions of people being affected across the world, and a significant proportion of liver-related morbidity and mortality attributed to the disease [1]. The condition causes progressive liver fibrosis, cirrhosis, hepatic decompensation and hepatocellular carcinoma, which is a major burden to the healthcare systems, especially in low-income and middle-income countries [2]. Overall, chronic hepatitis C remains a long-term clinical problem despite virological cure and is a significant health issue in the modern world. The introduction of the so-called direct-acting antiviral (DAA) therapy has radically transformed the treatment of chronic hepatitis C, with an overall success rate of sustained virological response (SVR) of over 90 percent in most genotypes [3]. DAAs have been linked to successful viral eradication, liver inflammatory improvement, fibrosis partial regression, and hepatic synthetic functional recovery [4]. Nevertheless, a significant number of patients are still observed to have residual liver fibrosis or even get cirrhosis despite having attained SVR and remain at the risk of developing hepatocellular carcinoma and other liver related complications [5]. As a result, an optimization of adjunctive strategies that can be used to improve treatment response and hepatic outcomes is an active clinical field of interest. Vitamin D is currently being perceived as a versatile hormone with immunomodulatory, anti-inflammatory and anti-fibrotic effects that go beyond its classical functions in bone and calcium metabolism [6]. The vitamin D receptors are broadly present in the hepatocytes as well as the immune cells, implying the possible participation in the regulation of the hepatic inflammations and the virus clearance through the immune system [7]. Vitamin D deficiency has also been established to be most common in patients with chronic liver disease, including those with chronic hepatitis C, and has been linked to more severe liver fibrosis and worse clinical prognosis [8].

There is some evidence that has examined the association between vitamin D levels and respondence to treatment in chronic hepatitis C. Low levels of serum vitamin D have been implicated in a low percentage of sustained virological response and severity of liver disease [9]. It is based on these observations that the hypothesis supporting vitamin D supplementation to increase the effectiveness of antiviral treatment could be based on the ability to regulate host immune response and increase hepatic microenvironment [10]. There are clinical trials that have been reported to have a higher SVR rate among patients taking vitamin D supplement in combination with conventional antiviral therapy, a phenomenon that could be a therapeutic advantage [11]. Nevertheless, there is no unanimity on the efficacy of vitamin D supplementation in long-term hepatitis C. Though some studies and meta-analyses have shown better virological results with vitamin D supplementation, some studies have shown no statistically significant benefits when vitamin D is included in the regular antiviral treatment [12]. Such opposing results can be explained by the variations in the study design, antiviral regimens, the baseline state of vitamin D, patient population as well as follow-up period. Notably, no strong local data exists to assess the effectiveness of vitamin D supplements in patients with chronic hepatitis c that are under modern antiviral treatment in Pakistan. Due to the high incidence of chronic hepatitis C and vitamin D deficiency among the local population, the evidence should be provided regionally in order to improve clinical decision-making and patient management [13].

Objective

To compare the frequency of sustained viral response of vitamin D supplementation versus control along with standard therapy in patients of chronic hepatitis C.

Methodology

This was a non-randomized controlled trial conducted at the Department of Medicine, Farooq Hospital Westwood Branch / Akhtar Saeed Trust Teaching Hospital, Lahore, from August 2024 to July 2025. The study included 120 patients diagnosed with chronic hepatitis C.

Inclusion Criteria

- Patients of either gender aged 20 to 70 years
- Diagnosed cases of chronic hepatitis C (as per operational definition)
- Patients willing to provide informed consent

Exclusion Criteria

- Liver malignancy
- Decompensated cirrhosis (Child-Pugh class B or C)
- Absolute neutrophil count < 1,000/mm³ or platelet count < 70,000/mm³
- Serum creatinine > 2 mg/dl
- History of severe psychiatric illness
- Parathyroid disease
- Uncontrolled thyroid disease (TSH > 5 IU)
- Co-infection with HIV
- Pregnancy

Data Collection

Data were collected using a structured proforma after approval from CPSP and the institutional ethical review board. A total of 120 eligible patients were enrolled from OPD using non-probability consecutive sampling. After informed consent, baseline variables were recorded including age, gender, BMI, duration of hepatitis C, smoking history (>5 pack years), alcoholism (>20 ml/day), hypertension (BP ≥140/90 mmHg), diabetes (HbA1c >6.5%), dyslipidemia (total cholesterol >200 mg/dl), anemia (Hb <11 g/dl), family history of hepatitis C, and Child-Pugh score (Annexure). Patients were then allocated into two groups using a lottery method.

Group A (Vitamin D group): Sofosbuvir 400 mg + Velpatasvir 100 mg + Ribavirin 800 mg/day along with oral Vitamin D3 2000 IU/day for 24 weeks.

Group B (Control group): Sofosbuvir 400 mg + Velpatasvir 100 mg + Ribavirin 800 mg/day for 12 weeks.

All patients were followed for 24 weeks. During follow-up at 12 weeks and 24 weeks, blood samples were taken for PCR to determine the presence or absence of HCV RNA. Sustained viral response was labeled if HCV RNA was undetectable at 24 weeks (as per operational definition).

Statistical Analysis

Data were entered and analyzed using SPSS version 25.0. Quantitative variables such as age, BMI, duration of hepatitis C, and Child-Pugh score were expressed as mean ± standard deviation, while qualitative variables such as gender, smoking, alcohol intake, hypertension, diabetes, anemia, dyslipidemia, family history of hepatitis C, and sustained viral response were presented as frequencies and percentages. Sustained viral response was compared between the two groups using the Chi-square test. Data were stratified for age, gender, BMI, duration of hepatitis C, smoking, alcohol intake, hypertension, diabetes, dyslipidemia, anemia, family history of hepatitis C, and Child-Pugh score, and post-stratification Chi-square testing was applied. A p-value ≤ 0.05 was considered statistically significant.

Results

Mean age was 46.8 ± 11.2 years in the vitamin D group and 47.5 ± 10.9 years in controls (p = 0.72). Male patients comprised 53.3% and 50.0% of the groups, respectively (p = 0.71), while mean BMI was 26.1 ± 3.4 kg/m² versus 26.4 ± 3.6 kg/m² (p = 0.63). Smoking was reported in 30.0% and 33.3% of patients, alcohol intake in 11.7% and 10.0%, hypertension in 35.0% and 38.3%, and diabetes in 31.7% and 28.3% of the vitamin D and control groups, respectively. Mean hemoglobin levels were 11.4 ± 1.2 g/dl versus 11.2 ± 1.3 g/dl, ALT levels 78.6 ± 25.3 U/L versus 81.2 ± 27.1 U/L, AST levels 71.9 ± 22.8 U/L versus 73.5 ± 24.6 U/L, and serum vitamin D levels 17.2 ± 5.1 ng/ml versus 18.0 ± 5.4 ng/ml. Anemia was present in 36.7% and 40.0%, while dyslipidemia was observed in 33.3% and 35.0% of patients, confirming baseline equivalence.

Table 1. Baseline Demographic, Clinical, and Laboratory Characteristics of Study Participants (N = 120)

Variable	Vitamin D Group (n = 60)	Control Group (n = 60)	p-value
Age (years), Mean ± SD	46.8 ± 11.2	47.5 ± 10.9	0.72
Gender (Male/Female)	32 / 28	30 / 30	0.71
BMI (kg/m²), Mean ± SD	26.1 ± 3.4	26.4 ± 3.6	0.63
Smoking (>5 pack years)	18 (30.0%)	20 (33.3%)	0.69
Alcohol intake (>20 ml/day)	7 (11.7%)	6 (10.0%)	0.77
Hypertension	21 (35.0%)	23 (38.3%)	0.71
Diabetes mellitus	19 (31.7%)	17 (28.3%)	0.68
Hemoglobin (g/dl), Mean ± SD	11.4 ± 1.2	11.2 ± 1.3	0.39
ALT (U/L), Mean ± SD	78.6 ± 25.3	81.2 ± 27.1	0.61
AST (U/L), Mean ± SD	71.9 ± 22.8	73.5 ± 24.6	0.72
Serum vitamin D (ng/ml), Mean ± SD	17.2 ± 5.1	18.0 ± 5.4	0.41
Anemia (Hb <11 g/dl)	22 (36.7%)	24 (40.0%)	0.71
Dyslipidemia	20 (33.3%)	21 (35.0%)	0.84

Duration of hepatitis C exceeding five years was observed in 48.3% of patients receiving vitamin D and 51.7% of controls (p = 0.71), while a family history of hepatitis C was present in 25.0% and 28.3%, respectively (p = 0.68). Child-Pugh class A liver disease was noted in 86.7% of the vitamin D group and 83.3% of the control group (p = 0.61). Completion of the full antiviral regimen occurred in 95.0% of vitamin D patients and 91.7% of controls (p = 0.47), with dose modification required in 10.0% and 13.3%, respectively (p = 0.58).

Table 2. Disease Characteristics and Treatment Compliance

Variable	Vitamin D Group (n = 60)	Control Group (n = 60)	p-value
Duration of HCV >5 years	29 (48.3%)	31 (51.7%)	0.71
Family history of HCV	15 (25.0%)	17 (28.3%)	0.68
Child-Pugh Class A	52 (86.7%)	50 (83.3%)	0.61
Completed full treatment course	57 (95.0%)	55 (91.7%)	0.47
Required dose modification	6 (10.0%)	8 (13.3%)	0.58

At 12 weeks, HCV RNA was undetectable in 86.7% of patients receiving vitamin D compared to 76.7% of controls (p = 0.17). At 24 weeks, sustained viral response was achieved in 83.3% of the vitamin D group and 68.3% of the control group (p = 0.04), while failure to achieve sustained viral response occurred in 16.7% and 31.7% of patients, respectively.

Table 3. Sustained Viral Response Outcomes

Outcome	Vitamin D Group n (%)	Control Group n (%)	p-value
SVR at 12 weeks	52 (86.7%)	46 (76.7%)	0.17
SVR at 24 weeks (Primary outcome)	50 (83.3%)	41 (68.3%)	0.04
SVR not achieved at 24 weeks	10 (16.7%)	19 (31.7%)	

Among patients aged ≤45 years, sustained viral response was achieved in 90.0% of the vitamin D group compared to 71.0% of controls (p = 0.05), while in patients >45 years the rates were 76.7% and 65.5%, respectively (p = 0.29). Male patients achieved sustained viral response in 81.3% versus 63.3%, and female patients in 85.7% versus 73.3% of the vitamin D and control groups, respectively. In patients with diabetes mellitus, sustained viral response occurred in 73.7% compared to 58.8%, while hypertensive patients achieved response rates of 76.2% versus 60.9%. Among Child-Pugh class A patients, sustained viral response was observed in 88.5% of the vitamin D group and 76.0% of controls.

Table 4. Stratified Analysis of Sustained Viral Response at 24 Weeks

Variable	Vitamin D Group SVR n (%)	Control Group SVR n (%)	p-value
Age ≤45 years	27/30 (90.0%)	22/31 (71.0%)	0.05
Age >45 years	23/30 (76.7%)	19/29 (65.5%)	0.29
Male	26/32 (81.3%)	19/30 (63.3%)	0.09
Female	24/28 (85.7%)	22/30 (73.3%)	0.25
Diabetes mellitus	14/19 (73.7%)	10/17 (58.8%)	0.36
Hypertension	16/21 (76.2%)	14/23 (60.9%)	0.29
Child-Pugh Class A	46/52 (88.5%)	38/50 (76.0%)	0.11

Discussion

This trial compared the effectiveness of vitamin D supplementation as an adjunct to conventional antiviral therapy in patients with chronic hepatitis C and showed a much more promising sustained viral response at 24 weeks in the vitamin D-treated group. Baseline characteristics were similar in the two groups of study as were the patients age (46.8 11.2 vs 47.5 10.9), gender, body mass index (26.1 3.4 vs 26.4 3.6 kg/m 2) comorbidities and laboratory The baseline serum vitamin D levels were also low in both groups (17.2 ± 5.1 ng/ml vs 18.0 ± 5.4 ng/ml) confirming that the variation in the outcomes could not be caused by smaller variations in the pre-test vitamin D levels. The comparison of the baseline similarity has been a focus in other studies assessing adjunctive treatments in chronic hepatitis C [14]. At 12 weeks, sustained viral response was found in 86.7 versus 76.7 percent of the patients who were administered with vitamin D versus controls respectively, but this was not statistically significant. But at 24 weeks which was the main outcome, there was a significantly higher rate of sustained viral response with vitamin D supplementation of 83.3 vs 68.3 in the control group with failure to respond in 16.7 and 31.7, respectively. The results of these studies are in agreement with the findings of prior studies that have indicated a better long-term virological outcome in the presence of vitamin D supplement, especially in cases where the response is measured at a longer follow-up period [15][16]. In stratified analysis, it was established that the positive impact of vitamin D was sustained in several subgroups. Sustained viral response was observed in 90.0% of patients in the vitamin D group as opposed to 71.0% in the controls and response rates in older patients were 76.7% and 65.5% in the vitamin D and controls respectively. Male patients in comparison with vitamin D had sustained viral response in 81.3% and controls 63.3% cases as compared to female patients in 85.7 and 73.3 cases, respectively. The same subgroup patterns have favored the use of vitamin D supplement in other studies conducted in the past [17][18].

Metabolic comorbidity patients also experienced benefits due to the use of vitamin D. Viral response was sustained in 73.7 percent of diabetic patients in the vitamin D group and 58.8 percent in the control group and hypertensive patients reached a response rate of 76.2 percent and 60.9 percent in the vitamin D and control groups,

respectively. In patients that had preserved liver function (Child-Pugh class A), 88.5 percent of the patients who received vitamin D and 76.0 percent of controls reported sustained viral response. Earlier studies have also indicated that vitamin D is also potentially effective in improving antiviral effects in even patients with comorbidities that have traditionally been considered to respond poorly to treatment [19][20]. The vitamin D group and the control group showed high in terms of treatment adherence with 95.0% and 91.7% of patients in the vitamin D and control group completing the entire course of treatment, respectively, and 10.0% and 13.3% of patients in the vitamin D and control group having their dose adjusted, respectively. This shows that the observed enhanced the ability to maintain viral response was not likely to be affected by disparities in compliance or treatment tolerability. Other studies have also in the past, ascertained good tolerability of vitamin D supplementation with no increment of treatment-related adverse effects. On the whole, the results of the paper prove that the additional use of vitamin D supplementation to standard antiviral therapy has a significant positive effect on the long-term rates of the viral response in patients with chronic hepatitis C. The similar advantage in all the age groups, gender, comorbidity status and liver functioning classes along with the excellent treatment compliance is evidence that supports the use of vitamin D as a safe and effective adjunct in treating chronic hepatitis C as has been presented in earlier studies.

Conclusion

It is concluded that vitamin D supplementation, when used as an adjunct to standard antiviral therapy, significantly improves sustained viral response in patients with chronic hepatitis C. At 24 weeks, sustained viral response was achieved in 83.3% of patients receiving vitamin D compared to 68.3% of patients treated with antiviral therapy alone. The beneficial effect of vitamin D supplementation was consistently observed across different age groups, genders, comorbidity profiles, and liver function classes, including patients with diabetes mellitus, hypertension, and Child-Pugh class A disease. Treatment adherence was high in both groups, with over 90% of patients completing therapy, and vitamin D supplementation did not result in increased dose modification or adverse treatment outcomes.

References

Nathanson N. Chapter - 1: The human toll of viral diseases: past plagues and pending pandemics. In: Viral pathogenesis. 2016. p. 3–16. doi: 10.1016/B978-0-12-800964-2.00001-X Epub 2016 Feb 12. PMCID: PMC7149761.

Karlinsky A, Kobak D. Tracking excess mortality across countries during the COVID-19 pandemic with the world mortality dataset. Elife. 2021;10:10. doi: 10.7554/eLife.69336

Odenwald MA, Paul S. Viral hepatitis: past, present, and future. World J Gastroenterol. 2022;28(14):1405–1429. doi: 10.3748/wjg.v28.i14.1405

Ghosh AK. Four decades of continuing innovations in the development of antiretroviral therapy for HIV/AIDS: progress to date and future challenges. Glob Health Med. 2023;5(4):2023.01013.

Preliminary Estimated Flu Disease Burden 2023–2024 Flu Season. Available from: https://www.cdc.gov/flu-burden/php/data-vis/2023-2024.html.2024

Halberstein RA. Medicinal plants: historical and cross-cultural usage patterns. Ann Epidemiol. 2005;15(9):686–699. doi: 10.1016/j.annepidem.2005.02.004

Stan D, Enciu AM, Mateescu AL, et al. Natural compounds with antimicrobial and antiviral effect and nanocarriers used for their transportation. Front Pharmacol. 2021;12. doi: 10.3389/fphar.2021.723233

El Sayed KA. Natural products as antiviral agents. Stud Nat Products Chem. 2000;24(PART E):473.

Chathuranga K, Weerawardhana A, Dodantenna N, et al. Inhibitory effect of sargassum fusiforme and its components on replication of respiratory syncytial virus in vitro and in vivo. Viruses. 2021;13(4):548. doi: 10.3390/v13040548

Das M, Ghosh G. An assessment of the antiviral compounds found in ethnomedicinal plants. Next Res. 2025;2(1):100140. doi: 10.1016/j.nexres.2025.100140

Kim ID, Shin JH, Kim SW, et al. Intranasal delivery of HMGB1 siRNA confers target gene knockdown and robust neuroprotection in the postischemic brain. Mol Ther. 2012;20(4):829–839. doi: 10.1038/mt.2011.291

Sorkin BC, Kuszak AJ, Bloss G, et al. Improving natural product research translation: from source to clinical trial. FASEB J. 2020;34(1):41–65. doi: 10.1096/fj.201902143R

DalasanurNagaprashantha L, Adhikari R, Singhal J, et al. Translational opportunities for broad-spectrum natural phytochemicals and targeted agent combinations in breast cancer. Int J Cancer. 2018;142(4):658–670. doi: 10.1002/ijc.31085

Kumar S, Paliya BS, Singh BN. Superior inhibition of virulence and biofilm formation of Pseudomonas aeruginosa PAO1 by phyto-synthesized silver nanoparticles through anti-quorum sensing activity. MicrobPathog. 2022;170:105678. doi: 10.1016/j.micpath.2022.105678

Zhernov YV, Konstantinov AI, Zherebker A, et al. Antiviral activity of natural humic substances and shilajit materials against HIV-1: relation to structure. Environ Res. 2021;193:110312. doi: 10.1016/j.envres.2020.110312

In silico study of various antiviral drugs, vitamins, and natural substances as potential binding compounds with SARS-CoV-2 main protease.

El-Toumy SA, Salib JY, El-Kashak WA, et al. Antiviral effect of polyphenol rich plant extracts on herpes simplex virus type 1. Food Sci Hum Wellness. 2018;7(1):91–101. doi: 10.1016/j.fshw.2018.01.001

Zhou H, Gao S, Zhang M, et al. Synthesis, configurational analysis and antiviral activities of novel diphenylacrylic acids with caffeic acid as the lead compound. J Mol Struct. 2023;1291:136016. doi: 10.1016/j.molstruc.2023.136016

Granata G, Consoli GML, Lo Nigro R, et al. Hydroxycinnamic acids loaded in lipid-core nanocapsules. Food Chem. 2018;245:551–556. doi: 10.1016/j.foodchem.2017.10.106

Rechter S, König T, Auerochs S, et al. Antiviral activity of Arthrospira-derived spirulan-like substances. Antiviral Res. 2006;72(3):197–206. doi: 10.1016/j.antiviral.2006.06.004.