Section: General Medicine

Original Research Article

CORRELATION BETWEEN SERUM 25-HYDROXYVITAMIN D CONCENTRATIONS AND CLINICAL OUTCOMES IN CHRONIC LIVER DISEASE

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Received *: 28/11/2025*
Received in revised form *: 14/01/2026*
Accepted *: 31/01/2026*

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DOI: 10.70034/ijmedph.2026.1.188

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (1); 1069-1073

ABSTRACT

Background: Chronic liver disease (CLD) is a progressive disease marked by compromised liver function and structural deterioration. Vitamin D insufficiency is commonly noted in CLD patients due to compromised hydroxylation in the liver, malabsorption, and diminished sunshine exposure. Reduced serum 25-hydroxyvitamin D [25(OH)D] concentrations have been linked to increased disease severity, comorbidities, and unfavorable clinical outcomes in these patients. **Aim:** This study aimed to estimate serum 25(OH)D levels in patients with chronic liver disease and evaluate their correlation with clinical outcomes.

Materials and Methods: This prospective observational study was carried out over seven months in the Department of General Medicine at Government Sivagangai Medical College. A total of 55 individuals diagnosed with CLD, according to clinical, biochemical, and imaging criteria, were included. Serum 25(OH)D concentrations were quantified utilizing standard chemiluminescent immunoassay methodologies. Patients were categorized based on vitamin D status (adequate, insufficient, and deficient), and their clinical outcomes—including liver disease severity, complication development, and hospitalization duration—were documented and studied. Statistical associations between serum vitamin D concentrations and clinical indicators were conducted.

Results: Of the 55 patients, the majority had low or insufficient serum levels of 25(OH)D. A notable negative connection was identified between serum vitamin D concentrations and illness severity, evaluated using the Child-Pugh score ($p < 0.05$). Patients with diminished vitamin D levels demonstrated increased incidences of sequelae including ascites, hepatic encephalopathy, and spontaneous bacterial peritonitis. Moreover, diminished 25(OH)D levels correlated with extended hospitalizations and inferior overall outcomes.

Conclusion: Vitamin D insufficiency is common in CLD and is associated with heightened disease severity and negative clinical outcomes. Routine evaluation of serum 25(OH)D concentrations may function as an effective prognostic indicator in individuals with CLD and assist in directing supplementation approaches to potentially enhance outcomes.

Keywords: Child-Pugh score, Chronic liver disease, complications, 25-hydroxyvitamin D, Vitamin D deficiency.

INTRODUCTION

Chronic liver disease (CLD) encompasses a range of progressive hepatic illnesses marked by sustained inflammation, fibrosis, and ultimately, hepatic dysfunction.[1] It includes illnesses such as chronic hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease, and cirrhosis, which combined result in substantial morbidity and mortality globally.[2]

The liver is integral to various metabolic and endocrine functions, including the hydroxylation of vitamin D to its principal circulating form, 25-hydroxyvitamin D [25(OH)D]. Thus, prolonged liver

dysfunction can cause impaired vitamin D metabolism, leading to shortage or insufficiency.[3,4]
Vitamin D, historically acknowledged for its function in calcium regulation and skeletal health, has surfaced as a multifaceted hormone affecting immunological modulation, inflammation, and cellular growth. In the realm of liver illness, vitamin D insufficiency has been associated with the advancement of fibrosis, heightened vulnerability to infections, and inferior overall results.[5]
The liver hydroxylates cholecalciferol (vitamin D3) to 25-hydroxyvitamin D, which is then converted in the kidneys to the physiologically active 1,25-dihydroxyvitamin D. Any impairment in liver function can diminish the synthesis of 25(OH)D, resulting in systemic insufficiency.[6]
Epidemiological studies indicate a significant frequency of vitamin D deficiency in patients with CLD, frequently surpassing 70% in cases of severe liver disease.[7] Factors contributing to insufficiency encompass diminished hepatic production, poor intestine absorption resulting from cholestasis, inadequate sun exposure, malnutrition, and associated comorbidities.[8]
Reduced serum 25(OH)D concentrations have been correlated with increased severity of liver dysfunction, as indicated by clinical scoring systems such the Child-Pugh and Model for End-Stage Liver Disease (MELD) scores.[9] Moreover, deficiency has been associated with consequences such as ascites, hepatic encephalopathy, infections, and osteoporosis, all of which considerably affect patient quality of life and survival.[10]
Although the importance of vitamin D for liver function is becoming more well recognized, less is known about its prevalence and prognostic relevance in Indian CLD patients. Comprehending the relationship between blood 25(OH)D levels and clinical outcomes may yield significant insights into disease development and function as a possible biomarker for risk stratification.
Timely detection of insufficiency may provide a pathway for therapeutic intervention, since supplementation could alleviate problems, enhance immunological function, and potentially decelerate the progression of liver disease. The study is to evaluate vitamin D status in connection with disease severity and consequences, so enhancing the existing knowledge about the prognostic importance of vitamin D in CLD and investigating novel techniques for optimizing patient care.

Aims and Objectives

- To estimate serum 25(OH)D levels in patients with chronic liver disease and evaluate their correlation with clinical outcomes.

MATERIALS AND METHODS

This was a prospective observational study conducted over a period of seven months in the Department of General Medicine at Government Sivagangai Medical College, Sivagangai, Tamilnadu. The study aimed to evaluate serum 25-hydroxyvitamin D [25(OH)D] levels in patients with CLD and to correlate these levels with clinical outcomes.
A total of 55 patients diagnosed with CLD were enrolled in the study. Diagnosis of CLD was based on a combination of clinical evaluation, laboratory investigations, and imaging studies, including ultrasonography of the abdomen. Both male and female patients aged 18 years and above were considered for inclusion.

Inclusion Criteria

- Patients with confirmed CLD of any etiology (viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease, or cryptogenic cirrhosis).
- Age ≥18 years.
- Patients who provided informed written consent to participate in the study.

Exclusion Criteria

- Patients with acute liver failure.
- Individuals already receiving vitamin D supplementation or medications affecting vitamin D metabolism (e.g., anticonvulsants, steroids).
- Patients with chronic kidney disease, malabsorption syndromes, or other systemic illnesses affecting vitamin D levels.
- Pregnant or lactating women.

Demographic details, including age, sex, and relevant medical history, were recorded for all participants. Detailed clinical evaluation was performed, including assessment of liver disease severity using the Child-Pugh classification. History of complications such as ascites, hepatic encephalopathy, variceal bleeding, and spontaneous bacterial peritonitis was noted.
Blood samples were collected from each participant under aseptic conditions. Serum was separated and analyzed for 25-hydroxyvitamin D [25(OH)D] levels using a chemiluminescent immunoassay method. Additional routine investigations included complete blood count, liver function tests (AST, ALT, ALP, bilirubin), renal function tests, prothrombin time, and viral markers when indicated.
Serum 25(OH)D levels were categorized according to standard reference ranges:

- Sufficient: ≥30 ng/mL
- Insufficient: 20–29 ng/mL
- Deficient: <20 ng/mL

The primary outcome was the correlation between serum 25(OH)D levels and severity of liver disease (Child-Pugh score). Secondary outcomes included the association of vitamin D levels with clinical complications, duration of hospitalization, and overall prognosis.
Data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages.

Correlation between serum 25(OH)D levels and clinical parameters was assessed using Pearson or Spearman correlation coefficients, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 55 patients with CLD were included in the study. The mean age of the participants was 52.6 ± 11.4 years, with a male predominance (n =36, 65.5%) compared to females (n = 19, 34.5%). The demographic and baseline clinical characteristics are shown in Table 1.

Table 1: Age and Sex Distribution of Study Population

Age Group (years)	Male (n=36)	Female (n=19)	Total (n=55)	Percentage (%)
18–30	3	2	5	9.1
31–45	9	5	14	25.5
46–60	14	7	21	38.2
>60	10	5	15	27.2

Serum 25(OH)D levels varied widely among the patients. The mean vitamin D level was 18.4 ± 7.3 ng/mL. Based on standard classification, 31 patients (56.4%) were deficient, 17 (30.9%) were insufficient, and only 7 (12.7%) had sufficient vitamin D levels. [Table 2]

Table 2: Serum 25(OH)D Status in Study Population

Vitamin D Status	Number of Patients	Percentage (%)
Deficient (<20 ng/mL)	31	56.4
Insufficient (20–29 ng/mL)	17	30.9
Sufficient (≥30 ng/mL)	7	12.7

There was a significant negative correlation between serum 25(OH)D levels and disease severity. Patients with severe liver disease (Class C) had the lowest vitamin D levels, highlighting its association with advancing liver dysfunction. [Table 3]

Table 3: Serum 25(OH)D Levels According to Child-Pugh Class

Child-Pugh Class	Number of Patients	Mean 25(OH)D (ng/mL) ± SD	p-value
A (Mild)	15	26.1 ± 3.4	<0.001*
B (Moderate)	25	17.8 ± 5.2	
C (Severe)	15	11.4 ± 2.8	

Vitamin D levels decreased progressively with increasing MELD score. Patients with high MELD scores had markedly lower 25(OH)D levels, indicating a strong association with liver disease severity. [Table 4]

Table 4: Serum 25(OH)D Levels According to MELD Score Category

MELD Score Category	Number of Patients	Mean 25(OH)D (ng/mL) ± SD	p-value
<10 (Low risk)	12	25.8 ± 4.1	<0.001*
10–19 (Moderate)	28	17.5 ± 5.0	
≥20 (High risk)	15	11.2 ± 3.0	

Vitamin D deficiency was significantly associated with higher rates of liver-related complications, indicating a potential prognostic role. [Table 5]

Table 5: Association Between Vitamin D Status and Clinical Complications

Complication	Deficient	Insufficient	Sufficient	p-value
Ascites	24/31 (77.4)	9/17 (52.9)	2/7 (28.6)	0.03*
Hepatic Encephalopathy	13/31 (41.9)	4/17 (23.5)	0/7 (0)	0.04*
Variceal Bleeding	9/31 (29.0)	3/17 (17.6)	0/7 (0)	0.05*

Patients with lower vitamin D levels had significantly longer hospital stays, suggesting poorer clinical outcomes in vitamin D-deficient individuals. [Table 6]

Table 6: Serum 25(OH)D Levels and Duration of Hospitalization

Vitamin D Status	Number of Patients	Mean Hospital Stay (days) ± SD	p-value
Deficient (<20 ng/mL)	31	12.6 ± 3.2	0.002*
Insufficient (20–29 ng/mL)	17	9.8 ± 2.7	
Sufficient (≥30 ng/mL)	7	7.1 ± 1.5	

DISCUSSION

The current study comprised 55 patients diagnosed with CLD, with a mean age of 52.6 ± 11.4 years, and a male predominance of 65.5% relative to 34.5% females. The age and sex distribution of the study population aligns with prior epidemiological studies, which indicates a higher prevalence of CLD among middle-aged adults and males, likely due to increased exposure to risk factors such as alcohol consumption and viral hepatitis within this demographic. The predominant age group among patients in the present study was 46–60 years, highlighting that liver disease typically presents clinically during middle age, when hepatic reserve diminishes and complications are more probable.

Serum 25-hydroxyvitamin D [25(OH)D] concentrations were significantly decreased in a substantial percentage of patients, with a mean value of 18.4 ± 7.3 ng/mL. Vitamin D deficiency (<20 ng/mL) was observed in 56.4% of patients, 30.9% exhibited insufficient levels (20–29 ng/mL), and merely 12.7% were vitamin D sufficient (≥30 ng/mL). The findings indicate a significant incidence of vitamin D deficiency in patients with CLD, aligning with previous research that identifies poor hepatic hydroxylation, malabsorption, diminished sun exposure, and nutritional inadequacies as contributing reasons. This insufficiency indicates the metabolic impairment associated with CLD and may worsen disease progression and associated consequences.

Koulagi M et al,[11] identified a 60.5% prevalence of Vitamin D insufficiency among participants with CLD in their investigation. Approximately 28.9% of the individuals had Vitamin D deficiency, whilst the remaining 10.5% demonstrated normal Vitamin D levels. The average Vitamin D levels among the participants were 22.15 ± 5.72 ng/mL. Raza M et al,[12] conducted a study with 178 individuals, revealing that 109 (61%) exhibited vitamin D deficiency, 37 (21%) shown vitamin D insufficiency, and 32 (18%) maintained adequate vitamin D levels. The findings of the study conducted by Zhang Y et al,[13] indicated that the levels of 25-(OH) D were significantly reduced in the progressive liver fibrosis subgroup compared to patients without progressive liver fibrosis and those with simple T2DM. Additionally, 25-(OH) D levels were lower in the subgroup without progressive liver fibrosis than in the simple T2DM group ($p < 0.01$ or $p < 0.05$).

The correlation between vitamin D levels and clinical consequences was significant. Patients with inadequate vitamin D levels exhibited markedly elevated rates of ascites (77.4%), hepatic encephalopathy (41.9%), and variceal haemorrhage (29%) in comparison to individuals with insufficient or adequate vitamin D levels, with p-values <0.05 for all sequelae. This suggests a possible prognostic function of vitamin D, as insufficiency seems to be associated with more severe clinical presentations of liver disease. Vitamin D may impact immunological regulation, inflammation, and fibrogenesis, hence influencing susceptibility to these problems.

Kumar P et al,[14] found that moderate to severe deficit of 25-OHD levels was substantially correlated with higher grades of HE, specifically grades 3 and 4 ($P < 0.0001$). A substantial negative association existed between 25-OHD levels and the progression of hepatic encephalopathy grades (Pearson's correlation coefficient $r = -0.354$; $P = 0.0003$). Yousuf A et al,[15] observed that patients with ascites ($p = 0.001$) and hepatic encephalopathy ($p = 0.038$) exhibited significantly reduced vitamin D levels.

The correlation between vitamin D levels and the severity of liver disease was validated by established scoring systems. Serum 25(OH)D concentrations diminished systematically across Child-Pugh classifications, with mean values of 26.1 ± 3.4 ng/mL in Class A, 17.8 ± 5.2 ng/mL in Class B, and 11.4 ± 2.8 ng/mL in Class C ($p < 0.001$).

The study by Jamil Z et al,[16] found that 88% of participants had either insufficient or deficient vitamin D levels, whereas only 12% had adequate levels ($p > 0.05$). Vitamin D levels were significantly associated with Child-Pugh class (contingency coefficient = 0.5, $p < 0.05$). The study conducted by Verma AK et al,[17] shown that patients with elevated Child Pugh scores are more likely to experience vitamin D deficiency and insufficiency compared to those with lower Child Pugh scores.

In a similar study, Ahmad MS et al,[18] found that 65.6% exhibited insufficient or deficient vitamin D levels, 23.2% had inadequate levels, and 11.2% maintained adequate vitamin D storage ($p > 0.05$). Vitamin D levels were significantly correlated with Child-Pugh class ($p < 0.05$).

Correspondingly, reduced vitamin D levels were noted in patients exhibiting elevated MELD scores, with average values of 25.8 ± 4.1 ng/mL for MELD <10, 17.5 ± 5.0 ng/mL for MELD 10–19, and 11.2 ± 3.0 ng/mL for MELD ≥20 ($p < 0.001$). The data indicate a significant negative association between vitamin D levels and the severity of liver failure, reinforcing the concept that vitamin D deficiency serves as both a marker and a potential contributor to disease development.

Patel JK et al,[19] noted that the mean vitamin D level was 19.89±8.64, seen in 15 patients with a MELD-Na score of ≤9, and that the mean vitamin D level decreased as the MELD-Na score increased. Reduced levels of vitamin D were substantially associated with elevated MELD-Na scores ($p<0.001$).

Longer hospital stays were also associated with vitamin D insufficiency. Patients with deficient levels experienced a mean hospitalization length of 12.6 ± 3.2 days, whereas those with insufficient levels had 9.8 ± 2.7 days, and patients with acceptable levels had 7.1 ± 1.5 days ($p = 0.002$). In the study conducted by Patel JK et al.19 low vitamin D levels were correlated with unfavourable outcomes, with a mean vitamin D level of 9.61±3.01 in deceased individuals compared to 16.52±7.47 in those who survived and were

discharged. This indicates that vitamin D levels may affect healing and overall prognosis, potentially through pathways related to immunological function, inflammation, and liver regeneration ability.

CONCLUSION

Vitamin D deficiency was frequent among CLD patients and is substantially correlated with greater illness severity, a higher incidence of comorbidities, and prolonged hospitalization. Evaluation of serum 25(OH)D concentrations may thus function as a valuable prognostic indicator and could guide supplementation approaches to enhance outcomes in this patient demographic. Regular monitoring and adequate repair of vitamin D insufficiency may constitute a simple yet powerful strategy to assist better clinical management of CLD.

Financial Support and Sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

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