

**Research Article****Serum Vitamin D and Parathyroid Hormone Status in Chronic Liver Disease and Their Relation to Disease Severity**

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**Abstract**

Chronic liver disease (CLD) is frequently associated with metabolic disturbances that affect calcium homeostasis and bone metabolism. Vitamin D deficiency is increasingly recognized as a common complication of CLD; however, concurrent alterations in parathyroid hormone (PTH) levels across both adult and pediatric populations remain inadequately characterized. The objective of this study was to evaluate serum vitamin D and PTH levels among adult and pediatric patients with CLD and determine their association with disease severity assessed by Child–Pugh classification and Model for End-Stage Liver Disease (MELD) score in adults, and Pediatric End-Stage Liver Disease (PELD) score in children.

A comparative cross-sectional study was conducted involving 240 participants, including 120 adult CLD patients, 30 pediatric CLD patients (0–12 years), and 90 healthy controls (60 adults and 30 pediatric controls). Serum 25-hydroxyvitamin D, intact PTH, calcium, phosphate, and liver function parameters were measured. Disease severity was categorized according to Child–Pugh classes A, B, and C in adults and PELD severity categories in pediatric patients. Statistical analyses were performed using SPSS version 26.0.

Mean serum vitamin D levels were significantly lower in both adult and pediatric CLD patients compared with their respective controls ( $p < 0.001$ ), whereas serum PTH levels were significantly elevated ( $p < 0.001$ ). Progressive reduction in vitamin D concentrations and corresponding increases

in PTH levels were observed with increasing disease severity. Vitamin D demonstrated significant negative correlations with MELD score in adults ( $r=-0.61$ ,  $p<0.001$ ) and PELD score in children ( $r=-0.56$ ,  $p<0.001$ ), while PTH exhibited positive correlations (adult  $r=0.58$ ,  $p<0.001$ ; pediatric  $r=0.54$ ,  $p=0.002$ ). These findings demonstrate that vitamin D deficiency and secondary hyperparathyroidism are strongly associated with increasing severity of CLD in both adults and children. Simultaneous assessment of vitamin D and PTH may provide additional prognostic information regarding disease progression and metabolic complications across all age groups with chronic liver disease

**Keywords:** Chronic liver disease; Vitamin D deficiency; Parathyroid hormone

### Introduction

Chronic liver disease (CLD) remains a major global health challenge and represents a significant cause of morbidity, mortality, and healthcare burden worldwide. The disease encompasses a broad spectrum of hepatic disorders characterized by progressive inflammation, fibrosis, architectural distortion, and eventual cirrhosis. Despite substantial advances in diagnostic and therapeutic strategies, complications associated with CLD continue to contribute significantly to reduced quality of life and adverse clinical outcomes. Beyond hepatic dysfunction, CLD exerts profound systemic effects involving endocrine, metabolic, cardiovascular, and skeletal systems, highlighting the need for a comprehensive understanding of extrahepatic manifestations associated with disease progression [1-3].

Among the metabolic abnormalities observed in CLD, disturbances of vitamin D metabolism have gained increasing scientific attention. Vitamin D plays a fundamental role in calcium and phosphate homeostasis, bone mineralization, immune regulation, and cellular differentiation. The liver serves as a critical organ in vitamin D metabolism by facilitating the hydroxylation of vitamin D into 25-hydroxyvitamin D [25(OH)D], the major circulating form used to assess vitamin D status. Consequently, progressive hepatic dysfunction may impair vitamin D metabolism, resulting in reduced circulating concentrations and subsequent physiological consequences. Recent investigations have demonstrated that vitamin D deficiency is highly prevalent among patients with CLD and may contribute to disease progression through immunomodulatory and antifibrotic mechanisms [1-4].

Emerging evidence has suggested that vitamin D deficiency in CLD extends beyond skeletal complications and may influence hepatic inflammation, fibrosis, portal hypertension, susceptibility to infections, and overall survival. Reduced vitamin D levels have been associated with increased severity of fibrosis and poorer clinical outcomes in cirrhotic patients. Furthermore, vitamin D receptors are expressed in hepatic stellate cells, Kupffer cells, and hepatocytes, suggesting potential regulatory functions in hepatic injury and repair processes. These observations have prompted growing interest in exploring the clinical significance of vitamin D status as a potential biomarker of disease severity in chronic liver disorders [3-6].

Parathyroid hormone (PTH) represents another important component of calcium regulatory physiology that may be altered in CLD. Under physiological conditions, reductions in serum calcium or vitamin D concentrations stimulate PTH secretion, leading to increased calcium mobilization and maintenance of mineral homeostasis. Persistent vitamin D deficiency may result in secondary hyperparathyroidism, which contributes to bone demineralization and metabolic bone disease. Although elevated PTH concentrations have been documented in advanced liver disease, the relationship between PTH and severity of hepatic dysfunction remains incompletely understood. Moreover, available studies have produced inconsistent findings regarding the extent to which PTH reflects disease progression independently of vitamin D status [4-7].

Metabolic bone disease represents one of the most underrecognized complications of CLD. Osteopenia, osteoporosis, and increased fracture risk have been reported in patients with chronic hepatic disorders, particularly among those with cirrhosis. The pathogenesis is multifactorial and involves impaired vitamin D activation, reduced dietary intake, malabsorption, chronic inflammation, hormonal disturbances, reduced physical activity, and alterations in calcium metabolism. Consequently, simultaneous assessment of vitamin D and PTH may provide a more comprehensive evaluation of mineral metabolic disturbances in CLD and facilitate early identification of patients at risk of skeletal complications [5-8].

The Child–Pugh classification and MELD score are widely accepted tools for assessing disease severity and predicting prognosis in CLD. Previous investigations have demonstrated associations between declining vitamin D levels and increasing Child–Pugh class; however, the role of PTH in relation to these prognostic indices remains less clearly established. Furthermore, limited data are available regarding the combined assessment of vitamin D and PTH across different stages of disease severity, particularly in populations with a high burden of chronic liver disease. Clarification of these associations may enhance understanding of disease pathophysiology and identify clinically relevant biomarkers for risk stratification [6-9].

Recent studies published between 2022 and 2024 have highlighted the potential prognostic value of vitamin D deficiency in advanced liver disease, emphasizing associations with increased complications, hospitalizations, and mortality. Nevertheless, many studies have focused exclusively on vitamin D while overlooking concurrent alterations in PTH levels. This gap in knowledge limits comprehensive evaluation of calcium regulatory pathways and their potential contribution to disease progression. Investigation of both parameters simultaneously may therefore provide novel insights into metabolic disturbances accompanying chronic hepatic dysfunction [7-10].

The present study was designed to evaluate serum vitamin D and PTH concentrations in patients with chronic liver disease and determine their relationship with disease severity. By comparing biochemical profiles

across Child–Pugh classes and examining correlations with MELD scores, this study aimed to provide a more integrated assessment of mineral metabolism abnormalities in CLD. The findings may contribute to improved understanding of disease-related metabolic derangements and support the development of targeted strategies for early detection and management of high-risk patients [8-10].

### Methodology

A comparative cross-sectional analytical study was conducted at Nawaz sharif Medical College Gujrat/Aziz bhatti shaheed teaching hospital Gujrat. The study population comprised patients diagnosed with chronic liver disease attending outpatient clinics or admitted to medical wards during the study period. The diagnosis of chronic liver disease was established on the basis of clinical history, biochemical investigations, ultrasonographic findings, and relevant radiological evidence demonstrating chronic hepatic pathology persisting for more than six months. Healthy individuals without evidence of liver disease were recruited as controls.

Sample size was calculated using OpenEpi version 3.01 by considering a confidence level of 95%, study power of 80%, ratio of controls to cases of 1:2, and anticipated prevalence of vitamin D deficiency among chronic liver disease patients of 75% based on previous regional studies. The minimum calculated sample size was 166 participants. To compensate for potential incomplete data and non-response, the sample size was increased to 180 participants. The final study population consisted of 120 patients with chronic liver disease and 60 healthy controls.

Patients with chronic liver disease were further stratified according to Child–Pugh classification into Child–Pugh A (n=40), Child–Pugh B (n=40), and Child–Pugh C (n=40). Healthy controls were age- and sex-matched as closely as possible to minimize confounding variables.

Inclusion criteria comprised adults aged 18–70 years with confirmed chronic liver disease of any etiology and willingness to participate in the study. Control participants included apparently healthy individuals with normal liver function tests and no history of chronic systemic disease. Exclusion criteria included patients receiving vitamin D supplementation during the preceding six months, chronic kidney disease, primary hyperparathyroidism, malignancy, thyroid disorders, pregnancy, chronic corticosteroid therapy, active bone diseases, previous liver transplantation, acute liver failure, and refusal to participate.

All eligible participants received a detailed explanation regarding study objectives and procedures. Verbal informed consent was obtained before enrollment. Confidentiality of patient information was maintained throughout the study. Ethical approval was obtained from the Institutional Review Board prior to commencement of data collection and all procedures complied with the ethical principles outlined in the Declaration of Helsinki.

Demographic information including age, sex, body mass index, duration of liver disease, and etiology of chronic liver disease was recorded using a structured data collection form. Clinical examination findings and laboratory parameters were documented. Disease severity was assessed using Child–

Pugh classification and MELD score calculations.

Following overnight fasting, venous blood samples were collected under aseptic conditions. Serum 25-hydroxyvitamin D concentrations were measured using chemiluminescent immunoassay. Intact parathyroid hormone levels were determined using electrochemiluminescence immunoassay techniques. Serum calcium, phosphate, albumin, bilirubin, alanine aminotransferase, aspartate aminotransferase, international normalized ratio, and creatinine were analyzed using standardized automated laboratory methods. Quality control measures were implemented according to laboratory protocols.

Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), and sufficient ( $\geq$ 30 ng/mL). Secondary hyperparathyroidism was defined according to laboratory reference ranges for intact PTH concentrations. All laboratory assessments were performed in the same institutional laboratory to ensure consistency and minimize analytical variability.

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Quantitative variables

were expressed as mean  $\pm$  standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using independent t-test and one-way analysis of variance (ANOVA) with post hoc analysis where appropriate. Chi-square test was used for categorical variables. Pearson correlation analysis was applied to determine relationships between vitamin D levels, PTH concentrations, Child–Pugh score, and MELD score. A p-value of less than 0.05 was considered statistically significant.

### Results

A total of 180 participants were enrolled, including 120 patients with chronic liver disease (CLD) and 60 healthy controls. Among CLD patients, 40 were classified as Child–Pugh A, 40 as Child–Pugh B, and 40 as Child–Pugh C. The mean age of the study population was  $49.8 \pm 11.4$  years. No statistically significant difference was observed in age, sex distribution, or body mass index between controls and CLD patients ( $p > 0.05$ ). However, significant differences were observed in serum vitamin D, PTH, calcium, albumin, bilirubin, and MELD scores across study groups.

**Table 1. Demographic and baseline characteristics of study participants**

| Variable                 | Controls (n=60) | CLD Patients (n=120) | p-value |
|--------------------------|-----------------|----------------------|---------|
| Age (years)              | 48.6 $\pm$ 10.2 | 50.4 $\pm$ 11.8      | 0.294   |
| Male, n (%)              | 35 (58.3)       | 74 (61.7)            | 0.661   |
| Female, n (%)            | 25 (41.7)       | 46 (38.3)            | 0.661   |
| BMI (kg/m <sup>2</sup> ) | 25.8 $\pm$ 3.1  | 24.9 $\pm$ 3.7       | 0.102   |
| Duration of CLD (years)  | —               | 5.2 $\pm$ 2.8        | —       |
| Viral Hepatitis, n (%)   | —               | 67 (55.8)            | —       |

| Variable                   | Controls (n=60) | CLD Patients (n=120) | p-value |
|----------------------------|-----------------|----------------------|---------|
| NAFLD-related CLD, n (%)   | —               | 31 (25.8)            | —       |
| Alcohol-related CLD, n (%) | —               | 22 (18.4)            | —       |
| Serum Vitamin D (ng/mL)    | 32.4 ± 6.8      | 16.9 ± 7.1           | <0.001  |
| Serum PTH (pg/mL)          | 42.7 ± 10.3     | 79.5 ± 24.8          | <0.001  |

Patients with CLD demonstrated markedly lower vitamin D levels and significantly higher PTH concentrations compared with healthy controls. Demographic characteristics were comparable between groups, minimizing confounding effects.

**Table 2. Comparison of biochemical parameters according to Child–Pugh classification**

| Parameter         | Child A (n=40) | Child B (n=40) | Child C (n=40) | p-value |
|-------------------|----------------|----------------|----------------|---------|
| Vitamin D (ng/mL) | 22.8 ± 5.6     | 16.1 ± 4.9     | 11.7 ± 3.8     | <0.001  |
| PTH (pg/mL)       | 61.3 ± 13.4    | 79.8 ± 16.2    | 97.4 ± 19.6    | <0.001  |
| Calcium (mg/dL)   | 8.9 ± 0.5      | 8.4 ± 0.6      | 7.8 ± 0.7      | <0.001  |
| Albumin (g/dL)    | 3.6 ± 0.4      | 3.0 ± 0.5      | 2.4 ± 0.4      | <0.001  |
| Bilirubin (mg/dL) | 1.7 ± 0.6      | 3.2 ± 1.1      | 6.4 ± 2.0      | <0.001  |
| MELD Score        | 10.9 ± 2.4     | 17.1 ± 3.8     | 24.7 ± 5.2     | <0.001  |

A progressive decline in vitamin D and calcium concentrations was observed with worsening liver disease severity. Conversely, PTH levels increased significantly from Child–Pugh A to Child–Pugh C, indicating increasing metabolic dysregulation.

**Table 3. Correlation of Vitamin D and PTH with disease severity indices**

| Variable  | MELD Score (r) | p-value | Child-Pugh Score (r) | p-value |
|-----------|----------------|---------|----------------------|---------|
| Vitamin D | -0.61          | <0.001  | -0.67                | <0.001  |
| PTH       | 0.58           | <0.001  | 0.63                 | <0.001  |
| Calcium   | -0.49          | <0.001  | -0.52                | <0.001  |
| Albumin   | -0.56          | <0.001  | -0.59                | <0.001  |

Vitamin D exhibited a strong negative correlation with both MELD and Child–Pugh scores, whereas PTH demonstrated a significant positive correlation. These findings indicate that worsening hepatic dysfunction is associated with progressive vitamin D depletion and compensatory hyperparathyroidism.

**Table 4. Pediatric (0–12 years) Demographic and Baseline Characteristics**

| Variable                        | Pediatric Controls<br>(n=30) | Pediatric CLD Patients<br>(n=30) | p-value |
|---------------------------------|------------------------------|----------------------------------|---------|
| Age (years)                     | 7.1 ± 3.2                    | 7.6 ± 3.4                        | 0.548   |
| Male, n (%)                     | 17 (56.7)                    | 18 (60.0)                        | 0.793   |
| Female, n (%)                   | 13 (43.3)                    | 12 (40.0)                        | 0.793   |
| Weight (kg)                     | 24.8 ± 8.1                   | 23.2 ± 7.5                       | 0.421   |
| Duration of CLD (years)         | —                            | 2.8 ± 1.6                        | —       |
| Biliary Atresia, n (%)          | —                            | 12 (40.0)                        | —       |
| Autoimmune Liver Disease, n (%) | —                            | 7 (23.3)                         | —       |
| Metabolic Liver Disease, n (%)  | —                            | 6 (20.0)                         | —       |
| Other Etiologies, n (%)         | —                            | 5 (16.7)                         | —       |
| Serum Vitamin D (ng/mL)         | 34.6 ± 7.2                   | 18.3 ± 6.4                       | <0.001  |
| Serum PTH (pg/mL)               | 39.5 ± 8.9                   | 71.2 ± 18.7                      | <0.001  |
| Calcium (mg/dL)                 | 9.5 ± 0.4                    | 8.6 ± 0.6                        | <0.001  |

**Interpretation:** Pediatric CLD patients demonstrated significantly lower serum vitamin D and calcium levels and significantly higher PTH concentrations compared with healthy pediatric controls.

**Table 5. Biochemical Parameters According to Pediatric Disease Severity (PELD Categories)**

| Parameter         | Mild PELD<br>(n=10) | Moderate PELD<br>(n=10) | Severe PELD<br>(n=10) | p-value |
|-------------------|---------------------|-------------------------|-----------------------|---------|
| Vitamin D (ng/mL) | 23.7 ± 4.8          | 17.6 ± 4.1              | 12.5 ± 3.6            | <0.001  |
| PTH (pg/mL)       | 58.9 ± 11.5         | 71.4 ± 13.8             | 86.8 ± 15.4           | <0.001  |
| Calcium (mg/dL)   | 9.0 ± 0.4           | 8.5 ± 0.5               | 8.0 ± 0.6             | <0.001  |
| Albumin (g/dL)    | 3.5 ± 0.4           | 2.9 ± 0.4               | 2.3 ± 0.3             | <0.001  |
| Bilirubin (mg/dL) | 1.9 ± 0.7           | 4.1 ± 1.3               | 7.2 ± 2.1             | <0.001  |
| PELD Score        | 4.8 ± 1.9           | 12.7 ± 2.8              | 22.3 ± 4.5            | <0.001  |

Table 6. Correlation of Vitamin D and PTH with PELD Score in Pediatric CLD

| Variable  | PELD Score (r) | p-value |
|-----------|----------------|---------|
| Vitamin D | -0.56          | 0.002   |
| PTH       | 0.54           | 0.002   |
| Calcium   | -0.47          | 0.009   |
| Albumin   | -0.51          | 0.004   |

**Interpretation:** Vitamin D levels decreased significantly with increasing PELD score, while PTH levels increased, indicating worsening metabolic disturbances with progressive pediatric liver disease.

## Discussion

The present study demonstrated a significant reduction in serum vitamin D concentrations among patients with chronic liver disease compared with healthy controls. Simultaneously, serum parathyroid hormone levels were markedly elevated in CLD patients, indicating disruption of calcium–vitamin D homeostasis. The findings support the concept that metabolic abnormalities accompanying chronic liver disease extend beyond hepatic dysfunction and involve complex endocrine adaptations affecting mineral metabolism. These observations are consistent with contemporary evidence reporting a high prevalence of vitamin D deficiency in cirrhotic populations and emphasizing its clinical relevance as a marker of disease burden [11-12].

A notable finding of the current investigation was the progressive decline in serum vitamin D levels across Child–Pugh classes. Patients

classified as Child–Pugh C exhibited the lowest vitamin D concentrations, while Child–Pugh A patients maintained comparatively higher levels. This gradient suggests a close relationship between hepatic functional reserve and vitamin D metabolism. The liver plays an essential role in hydroxylation of vitamin D to 25-hydroxyvitamin D, and progressive hepatocellular damage may impair this process. Furthermore, reduced nutritional intake, malabsorption, diminished sunlight exposure, and chronic inflammation may contribute to worsening vitamin D deficiency in advanced disease stages [11-13].

The study also demonstrated significantly elevated PTH concentrations in patients with severe liver disease. Mean PTH levels increased progressively from Child–Pugh A to Child–Pugh C, suggesting activation of compensatory endocrine mechanisms secondary to vitamin D depletion and altered

calcium homeostasis. Secondary hyperparathyroidism may therefore represent an important but underrecognized manifestation of chronic liver disease. Similar findings have been reported in recent studies where elevated PTH concentrations were associated with impaired bone metabolism and increased fracture risk among cirrhotic patients [13-15].

The observed inverse relationship between vitamin D levels and MELD score further strengthens the hypothesis that vitamin D status reflects disease severity. The significant negative correlation identified in the present study indicates that lower vitamin D concentrations are associated with more advanced hepatic dysfunction. Previous investigations have similarly reported that vitamin D deficiency correlates with portal hypertension, hepatic decompensation, susceptibility to infection, and increased mortality risk. These observations support the potential utility of vitamin D as a supplementary prognostic biomarker in chronic liver disease [14-16].

An equally important observation was the positive correlation between PTH concentrations and disease severity indices. While vitamin D deficiency has been extensively studied, fewer investigations have examined the independent prognostic implications of PTH in chronic liver disease. The present findings suggest that elevated PTH may provide additional information regarding disease progression. Persistent secondary hyperparathyroidism may contribute to accelerated bone loss, muscle weakness, and reduced functional status, thereby increasing overall disease burden. Consequently, simultaneous evaluation of

vitamin D and PTH may offer a more comprehensive assessment than either parameter alone [15-17].

Serum calcium levels demonstrated a significant decline with increasing Child–Pugh class, further supporting the presence of progressive disturbances in mineral metabolism. Hypocalcemia in advanced liver disease may result from hypoalbuminemia, impaired vitamin D activation, intestinal malabsorption, and altered hormonal regulation. The strong association between calcium abnormalities and disease severity identified in the present study reinforces the need for routine monitoring of mineral metabolic parameters in patients with advanced hepatic dysfunction [16-18].

A major strength of the present investigation is the simultaneous assessment of vitamin D, PTH, calcium status, and established prognostic indices in a well-characterized CLD population. Unlike several previous studies that focused primarily on vitamin D deficiency, the current study provides evidence that secondary hyperparathyroidism progresses alongside worsening liver disease and may have independent clinical significance. These findings address an important knowledge gap and suggest that combined assessment of vitamin D and PTH may improve risk stratification and facilitate earlier intervention for metabolic complications. Future multicenter prospective studies are warranted to determine whether correction of vitamin D deficiency and associated hyperparathyroidism can favorably influence disease progression and clinical outcomes [18-20].

## Conclusion

Serum vitamin D deficiency and elevated parathyroid hormone levels are highly prevalent among patients with chronic liver disease and demonstrate significant associations with worsening Child–Pugh and MELD scores. Simultaneous assessment of vitamin D and PTH provides valuable insight into disease severity and metabolic dysfunction. These findings address an important prognostic gap and support incorporation of mineral metabolic evaluation into routine clinical assessment of chronic liver disease patients.

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