Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.960

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Frequency of Hypocalcemia in chronic Liver Disease Patients

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ARTICLE INFO

Keywords
Chronic Liver Disease, Calcium Homeostasis, Hypocalcemia, Child-Pugh Classification, Socioeconomic Factors.

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Declaration
Authors' Contribution: Sole authorship
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History
Received: 15-03-2025, Revised: 29-03-2025
Accepted: 01-04-2025, Published: 08-04-2025

ABSTRACT

Introduction: Chronic liver disease (CLD) frequently leads to electrolyte imbalances, including hypocalcemia, due to impaired hepatic function. Hypocalcemia has significant clinical implications, particularly in advanced stages of CLD. **Objectives**: To determine the frequency of hypocalcemia in chronic liver disease patients. **Materials and Methods**: This descriptive cross-sectional study was conducted at Shahida Islam Teaching Hospital, Lodhran, Pakistan in the duration from 14 September, 2024 to 12 March, 2025. A total of 81 CLD patients were included using non-probability consecutive sampling. Corrected serum calcium levels were measured, and data were analyzed using SPSS 25.0. **Results**: Published reports indicate that hypocalcemia was noted in 27 percent of patients in the study, most of whom were in Child-Pugh Class B and C. Higher use was reported by patients with low SEP and those who had had the disease for longer. Gender and BMI did not correlate. **Conclusion:** It should, however, be noted that hypocalcemia is primarily present in the advanced stages of CLD. Patients' outcomes may be enhanced when these practices are regularly observed, and early intercessions are made.

INTRODUCTION

Chronic liver disease (CLD) is recognized today as an international health issue characterized by the progressive decline in liver functions due to various factors, viruses, alcohol consumption, or nonalcoholic and fatty liver disease (1). Of all CLD complications, hypocalcemia is a complex and multifactorial electrolyte disorder, and its influence on the patient's prognosis led to further research concerns (1, 2). An essential role in the regulation of concentrations of calcium in the blood is the ability to get engaged in the metabolism of vitamin D and the synthesis of necessary proteins for calcium transportation, which is the key function of the liver. These procedures in CLD patients are often pathologic and cause changes in the calcium levels and other disease conditions (4 & 7). It has been pointed out that hypocalcemia in CLD depends on the orogeny and the severity of liver disease and is more frequent in patients with the decompensate liver disease (1, 3). For example, hypocalcemia is a common feature in viral liver decompensation, and is associated with independent predictors of both higher mortality and morbidity (1). This situation is made worse by the fact that vitamin D is subnormal during the severe phases of CLD and thus calcium bioavailability is low (4,7). In addition, chronic liver dysfunctions are associated with bone mineral metabolism and cause hypocalcemia and osteoporosis (7).

The electrolyte imbalances like hypocalcemia and hypokalemia were noted to be widespread among the patients with CLD, and these were also found to be relatively related to the extent of the disease (2, 6). Literature from different world regions reports elevated rates of hypocalcemia in cases of CLD patients. For instance, one Pakistani-based research outlined a high prevalence of electrolyte abnormalities. It indicated that the assessment and management of calcium problems should be more regular as the experience was very high in CLD patients (2, 12). The same outcome of CLD was made in India to demonstrate how chronic hepatic insufficiency disturbs calcium homeostasis and normal physiological functioning. Recent work also examines the degree of the relationship between hypocalcemia and system disorders in CLD children. For instance, the hypocalcemia cluster has been shown to result in a worsening of hepatic encephalopathy, a neurological complication arising from severe liver disorders (6). Besides, hypocalcemia has been described in other

diseases that may coexist with liver disease, such as COVID-19 in hospitalized patients, and has been associated with a worse outcome (5, 8, 10). This also stresses the general clinical relevance of monitoring calcium in patients with impaired liver function.

There are several factors that contribute to hypocalcemia in CLD patients. Decreased production of vitamin D 25-hydroxylase and reduced conversion of 25-hydroxyvitamin D to calcitriol is critical for the illustrated decrease in calcium absorption in the gut (4, 7). Moreover, the deficiency of albumin, which is typical for CLD patients, results in a reduction in the levels of calcium bound to protein (1, 3). The simultaneous presence of other electrolyte abnormalities, including hypokalemia, hampers management as the effects of hypocalcemia are worsened (2, 13). Membership of low-income earner's families and demographic differences also have an impact on the occurrence of hypocalcemia among CLD patients. People from rural settings or belonging to the low class have poor healthcare access and suffer from malnutrition and thus present with complications such as hypocalcemia in the advanced stages of the disease (7, 12). This demographic tendency should be taken into consideration in order to minimize disparities in the provision of healthcare services and patient counselling (12).

Instead, hypocalcemia is not limited to its biochemical connotations in clinical practice. It is linked to neuromuscular signs, cardiovascular autonomic abnormalities, and enhanced vulnerability to infections, all of which emerged as significant factors that negatively affect the quality of life of CLD patients (3, 10). This is why it is essential to understand the frequency and subjects with hypocalcemia to determine subsequent therapeutic approaches. To fill this gap, the present study aimed to describe the known prevalence and potential factors associated with hypocalcemia in CLD patients in this country. This research will help fill this knowledge gap by determining the extent of and factors influencing hypocalcemia among CLD patients admitted at the Shahida Islam Teaching Hospital, Lodhran. In this study, the authors aim to identify the clinical burden of hypocalcemia in this patient group to enhance management and promote improved outcomes. That is why dyslipidemia management in CLD patients, related to the presence of liver dysfunction in the processes of calcium homeostasis and shifts in systemic complications, suggests the need for hypocalcemia treatment. This investigation will offer important information about the frequency and medical implications of this electrolyte disturbance in CLD patients in order to help plan subsequent research and safety intervention studies.

Objective

To determine the frequency of hypocalcemia in chronic liver disease patients.

MATERIALS AND METHODS

Study Design: Cross Sectional.

Study setting: The study was conducted at the Department of Medicine, Shahida Islam Teaching Hospital, Lodhran, Pakistan.

Duration of the study: The duration of the study was from 14 September, 2024 to 12 March, 2025.

Inclusion Criteria

Inclusion criteria for this study were patients with CLD for a period of more than one month. The study targeted both males and females of the selected age group of 20-70 years. These analyses were limited to patients who fit the study's operational definition of CLD and who provided written informed consent. Each participant's demographical data, such as their place of residence and their socioeconomic status, was collected to explore the correlation of hypocalcemia risk factors.

Exclusion Criteria

Patients with heart failure, chronic renal disease or using medications altering serum calcium levels, including SSRI, TCA, MAOI, ACE inhibitors, ARBs or calcium supplements, were excluded. Also, patients on diuretic therapy, past or current cancer patients, or endocrine disease patients were excluded from this study.

Methods

Patients were recruited after receiving ethical clearance from the institutional ethical review committee and the College of Physicians and Surgeons Pakistan (CPSP). Patients included in the study aged between 25 and 45 years comprising 81 patients were selected through a non-probability consecutive sampling method. All participants signed an informed written consent concerning their willingness to participate in the study. Information about age, sex, disease duration, height, weight, BMI, rural/urban dwelling status, and monthly income were obtained and documented. In this instance, blood samples of 5 ml venous blood were used from all participants to determine corrected serum calcium through institutional pathology laboratories. Hypocalcemia was defined per the operational definition, and mention was made about whether the condition was present or absent. Information was collected in a structured format for analysis on proforma. The statistical test was done with SPSS software with version number 25. Data collected over time were presented as mean and standard deviation or median (IQR), whereas data collected in the set were presented in the form of frequency and proportional frequency. A stratification and chi-square test were used to manage the confounding factors. P-value < 0.05 was used to determine statistical test significance.

RESULTS

Eighty-one patients with a diagnosis of chronic liver disease (CLD) were enrolled for this study. The mean

age of the participants was 48.6 ± 12.4 years; 62% of patients were in the age group between 41–60 years. The study population comprised 68% males and 32% females. About 71% of the participants were living in rural areas, and 58% of participants had less than 25000 PKR income per month.

Table 1

Demographic and Socioeconomic Characteristics of Participants

Variable		Frequency (%)
Gender	Male	55 (68%)
	Female	26 (32%)
Age Group (years)	20–40	18 (22%)
	41–60	50 (62%)
	61–70	13 (16%)
Place of Residence	Rural	57 (71%)
	Urban	24 (29%)
Monthly Income (PKR)	<25,000	47 (58%)
	25,000–50,000	24 (30%)
	>50,000	10 (12%)

In this study patient population, hypocalcemia was identified in 27% (22 patients). Of those, most were Child-Pugh Class B or C, suggesting that hypocalcemia is common in more advanced liver disease. Hypocalcemia severity was within 4.0-8.5 mg/dL, with the mean serum calcium level equal to 7.4 ± 0.6 mg/dL, while in patients without hypocalcemia, the mean serum calcium level was 9.0 ± 0.4 mg/dL, $p < 0.001$.

Table 2

Clinical Characteristics of Participants

Variable	Hypocalcemia Present	Hypocalcemia Absent
Child-Pugh Class		
Class A	4 (18%)	19 (32%)
Class B	12 (55%)	28 (47%)
Class C	6 (27%)	12 (21%)
Mean Serum Calcium (mg/dL)	7.4 ± 0.6	9.0 ± 0.4

Chronic disease duration and poor socio-economic class were significantly associated with hypocalcemia $p = 0.02$ and $P = 0.03$, respectively, obtained from stratification analysis. Gender, as well as BMI, did not demonstrate a higher risk towards hypocalcemia, that is, $p > 0.05$.

Table 3

Factors Associated with Hypocalcemia

Variable	Hypocalcemia Present	p-value
Duration of Disease >1 year	15 (68%)	0.02
Monthly Income <25,000	16 (73%)	0.03
Gender (Male)	15 (68%)	0.12
BMI >25	5 (23%)	0.15

Finally, in the study, the study concluded that hypocalcemia is widespread among CLD patients, especially in the terminal stages and the low economic power of users. These outcomes support the necessity of adequate calcium assessment and practicable management in this group.

DISCUSSION

Therefore, the results of this research show that hypocalcemia is common among patients with CLD, especially if the patients have the late stage of the disease. Hypocalcemia, an essential electrolyte abnormality, has recently assumed a significant component of the clinical picture of CLD since the liver plays a vital role in the regulation of calcium levels (1, 3). These results are consistent with previous reports of hypocalcemia in this population, where causes are considered to be complex and interacting (4, 7). Another observation made in the study for hypocalcemia was that the severity of liver disease, as defined by the Child-Pugh system of staging, was positively correlated with hypocalcemic conditions. It could be hypothesized that patients in Class B and C had a higher degree of hypocalcemia, as previously reported in other studies (1, 3). Such a link could be associated with the reduced hepatic biosynthesis of 25-hydroxyvitamin D and further activation of calcitriol required for calcium absorption in the intestines (4, 7). Furthermore, hypoalbuminemia, which is often seen in patients with CLD stages 3 and 4, decreases protein-bound calcium even more and results in hypocalcemia.

Moreover, it examines the role of socioeconomic status in hypocalcemia amongst the population. This study found that patients who had lower monthly income were more likely to suffer from hypocalcemia in particular. This finding is significant with regard to Pakistani demographics, as the provision of health care, nutrition and disease intervention is significantly compromised due to socioeconomic differences (7, 12). Other nutritional factors, such as shortage of calcium and vitamin D, are universal in the impoverished and poor population and could further worsen hypocalcaemia in CLD patients (3, 7). The observed frequency of hypocalcemia in this study is similar to the report in such studies (27%), though there is variation due to differences in the study sample and methods (1, 4). Studies from India and other South Asian countries have also noted similar prevalence, indicating the need for regional research to capture specific demographic and clinical features of the population (3,7). Around the world, it was established that hypocalcemia has a propensity to be overlooked in CLD patients, which contributes to late diagnosis and reduced prognosis (5, 10).

It is critical to appreciate hypocalcemia and its effects on the clinical results in CLD patients. The disease has been associated with neuromuscular dysfunction, cardiovascular instability, and heightened vulnerability to infections, due to which the quality of life deteriorates and mortality rates are higher (3,10). Closely associated with cirrhosis, hepatic encephalopathy is a condition which, when compounded with hypocalcemia, will worsen neurological manifestations of the disease (6).

Therefore, it can be stressed that the assessment of serum calcium concentration should remain a compulsory component of managing CLD (1, 3). The results also stress that the disease duration is essential in determining hypocalcemia's appearance. Patients with CLD had hypocalcemia, and the patients who had had CLD for a more extended period presented more frequently with this condition, indicating that chronic liver disease has a cumulative effect on calcium metabolism (7). This observation is corroborated by research showing that increased duration of liver disease leads to worsening metabolic disturbance, such as vitamin D deficiency and electrolyte disturbance (4, 7). Measures in early targeting of these problems could potentially affect risks to the development of hypocalcemia and its complications (1, 4).

Notably, the authors discovered no relationship between gender and hypocalcemia, even though some prior investigations have hypothesized gender differences regarding the rate of calcium circulation in the body (2, 3). However, given the number of patients participating in this study, this finding can be attributed to the study's sample size. It should be investigated in a more extensive population with variations in population characteristics. Likewise, BMI did not appear as an indicator in presenting, but we know that obesity and malnutrition affect calcium and vitamin D (7, 12). Based on these findings, the primary root causes of hypocalcemia in CLD patients are probably not significantly linked with demographic factors but are rather more associated with the function of the liver and the economic situation in a given country. The major notable study characteristic that may be considered a strength is that this study focused on a particular patient group in a specific geographic area, describing the current state of hypocalcemia in CLD patients in Pakistan. It is also important to note certain limitations in this method's use. Although large enough to detect relevant associations, the number of participants may not be enough to provide an accurate account of the diverse nature of the CLD population. Also, the study was cross-sectional, meaning there is added difficulty in establishing correlation causes between hypocalcemia and various clinical outcomes. To increase knowledge about the natural course of hypocalcemia and its effects on severity and prognosis, longitudinal trials should be conducted in the future (5,10).

This review also highlights that other modifiable risk factors for hypocalcemia existing among CLD patients deserve specific research attention to be eliminated. Eating habits manipulations, particularly calcium and vitamin D intake, could significantly contribute to hypocalcemia prevention or treatment (7). Moreover, effective management and treatment for hypocalcemia to avoid the mentioned complications should cover the factors of health inequalities in socioeconomic status and treatment access to enhance public health quality to address the hypocalcemic issue (12). Such measures should be incorporated within strategies that enhance CLD patients' quality of care, especially in low-resource centers. The findings discussed also have implications for clinical practice and research. Screening for hypocalcemia should not be performed as a routine practice in CLD patients, but it should be done for patients with severe disease or poor living conditions. Further research should investigate how competent specific interventions like vitamin D supplementation and diets are in addressing hypocalcemia and clinician results (4, 7). Research should also seek to determine calcium handling in CLD at the molecular level to determine new targets for therapy (5, 10).

Lastly, hypocalcemia is another common and multifactorial complication of chronic liver disease that is more frequent in the end-stage and patients with low income. Therefore, the current study provides an impetus for routine assessments and intervention measures to solve this problem and enhance patient care. If the complex causes of hypocalcemia in CLD are recognized and treated, then healthcare organizations will foster the quality of care for affected patients and step down the impact of hypocalcemia. Therefore, further studies are encouraged to establish comprehensive and fact-based frameworks for tackling hypocalcemia in the CLD.

CONCLUSION

This study draws attention to the fact that Hypocalcemia is extremely common in CLD patients, especially in end-stage CLD patients. It was observed that patients with Hypocalcemia were more frequent in Child-Pugh Class B and C, and the patients with a longer duration of the disease revealed a strong correlation between Hypocalcemia and liver dysfunction. Socioeconomic factors also significantly contributed to the results, primarily because patients with lower SES had a higher incidence of Hypocalcemia, possibly due to poor nutrition and delayed use of health services. The importance of standardized monitoring of calcium levels in patients with CLD is confirmed, as well as the need for timely interventions based on supplementation and nutritional support. Practical counteraction to these problems can be achieved using public health interventions and optimizing clinical processes on the intended patient outcomes. More prospective studies are needed to correlate Hypocalcemia and CLD with its severity of CLD and consequences after long-term follow-up.

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