IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 8 Ser.4 (August. 2023), PP 23-28
www.iosrjournals.org

Comparison Of Serum Vitamin D Level AndCalcium Among The Patients With Chronic Liver Diseases And Healthy Individuals

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Abstract:
Introduction:*Chronic liver disease (CLD) is a progressive condition leading to hepatic fibrosis and cirrhosis. Patients with CLD often experience complications such as bleeding esophageal varices and ascites. Vitamin D deficiency is highly prevalent in CLD patients due to various factors, including reduced exposure, malabsorption, and impaired hepatic hydroxylation. Studies have consistently shown a significant deficiency of vitamin D in patients with CLD, emphasizing the importance of addressing this issue for improved skeletal health and immune function.*
Aim of the Study:*The aim of the study was to compare serum vitamin D levels and calcium levels between patients with chronic liver diseases and healthy individuals*
Methods:*This observational cross-sectional study took place at the Department of Gastroenterology, BSMMU, Dhaka, from April 2019 to March 2020. A total of 60 patients enrolled in this study, of them 30 had chronic liver disease who were admitted to the department and a comparison group comprising 30healthy attendants from the same department. Non-probability consecutive sampling was used, and data were collected, cleaned, and analyzed using SPSS version 22. Ethical clearance of this study was obtained from the Institutional Review Board (IRB) of BSMMU, Dhaka, Bangladesh.*
Results:*The study compared patients with chronic liver disease (CLD) to a healthy comparison group and found several key data findings. Patients with CLD had significantly higher mean age (49.76 ± 12.02 years) compared to the healthy group (37.96 ± 12.35 years) with a p-value of <0.001. Additionally, the CLD group had a higher proportion of males (70.0%) compared to the healthy group (46.7%) with a p-value of 0.042. Biochemical findings showed significant differences between the groups in serum albumin (p<0.001), serum calcium (p<0.001), serum creatinine (p=0.001), and platelet count (p=0.001). The study also revealed that a majority of CLD patients had deficient vitamin D levels (63.4%) compared to the healthy group (23.3%) with a p-value of 0.007. Finally, an association was observed between vitamin D levels and the severity of liver cirrhosis based on the Child-Turcotte-Pugh (CTP) classification with a p-value of 0.021.*
Conclusion:*The study revealed that chronic liver disease (CLD) is linked to advanced age, higher occurrence among males, decreased levels of serum albumin, calcium, and platelet count, along with a significant prevalence of vitamin D deficiency. Nonetheless, the limited sample size hinders the applicability of these findings to a broader population.*
Keywords:*Serum, Vitamin-D, Calcium, Chronic, liver*

Date of Submission: 04-08-2023 Date of Acceptance: 14-08-2023

I. INTRODUCTION

Chronic liver disease (CLD) is a progressive condition characterized by the long-term destruction and regeneration of the liver. It leads to hepatic fibrosis and, ultimately, cirrhosis, which is the final stage of chronic liver inflammation[1]. Cirrhosis is associated with various complications such as bleeding esophageal varices, ascites, and encephalopathy, primarily caused by portal hypertension and hepato-cellular failure[2]. Child's grade, which assesses hepato-cellular function based on factors like bilirubin, albumin, and prothrombin time, is commonly used to evaluate the severity of cirrhosis [3].Vitamin D plays a crucial role in regulating cell proliferation, differentiation, and immune function. It exhibits immunomodulatory, anti-inflammatory, and anti-fibrotic properties, making it essential for individuals with liver diseases [4]. However, vitamin D deficiency is highly prevalent among patients with chronic liver disease due to various factors. Reduced exogenous exposure, intestinal malabsorption, decreased endogenous production of vitamin D binding protein (DBP) and albumin in the liver, impaired hepatic hydroxylation of vitamin D, and increased catabolic removal of 25-hydroxyvitamin D [25(OH)D] contribute to this deficiency [5], [6].Studies have shown that up to 93% of patients with chronic liver disease have insufficient vitamin D levels, with approximately one-third of these individuals experiencing severe deficiency[7]. The prevalence of vitamin D deficiency is substantially higher among patients with chronic liver disease due to the role of vitamin D in calcium absorption. In these patients, the liver's impaired function and reduced production of DBP and albumin further contribute to the deficiency[5].To determine vitamin D deficiency or sufficiency, the circulating level of 25(OH)D, the major circulating form of vitamin D, is measured. Several assays, such as radioimmunoassay and competitive protein binding assays, are employed for this purpose. Vitamin D deficiency is defined as serum 25(OH)D levels below 20 ng/ml (50 nmol/L), while insufficiency is indicated by levels between 20 and 31 ng/ml [8], [9].Numerous studies conducted worldwide have aimed to assess the prevalence of vitamin D deficiency and serum calcium levels in patients with chronic liver disease. For instance, a study conducted in Iran compared serum vitamin D levels among 90 patients with CLD and 40 healthy controls. The study found a significantly higher prevalence of vitamin D deficiency in cirrhotic patients compared to non-cirrhotic individuals [10]. In Australia, researchers conducted a study involving 158 patients with chronic liver disease, and they found that 64% of these patients had a significant deficiency of 25(OH)D[11]. Similarly, studies conducted in different countries, including Australia and Italy, consistently reported substantial vitamin D deficiency among cirrhotic patients[12], [13]. Ultimately, chronic liver disease leads to cirrhosis and various complications, and it is associated with a high prevalence of vitamin D deficiency. Vitamin D plays a crucial role in skeletal health and immune function, making it essential for individuals with chronic liver disease. Measurement of serum 25(OH)D levels is crucial in assessing vitamin D status, as it accurately reflects an individual's vitamin D levels. Studies have consistently demonstrated a significant deficiency of vitamin D in patients with chronic liver disease, highlighting the importance of addressing this issue in clinical practice. The identification and management of vitamin D deficiency can help improve the skeletal health and immune function of patients with chronic liver disease.

II. METHODS

This observational cross-sectional study was conducted in the Department of Gastroenterology at BSMMU in Dhaka, Bangladesh, over a period from April 2019 to March 2020. The study included 60 patients, of them 30 had chronic liver disease who were admitted to the department and a comparison group comprising 30 healthy attendants from the same department. Non-probability consecutive sampling was used to select participants. Data collection involved obtaining relevant information from the participants, and no interventions or additional procedures were performed. The collected data were cleaned, entered into a computer, and analyzed using SPSS version 22. Descriptive statistics, such as means and standard deviations for numerical variables, and counts with percentages for categorical variables, were used for data presentation. Categorical variables were analyzed using the Chi-square tests and unpaired t tests with a significance level set at $p<0.05$. Ethical considerations were followed, including obtaining approval from the institutional review board, providing clear explanations to participants, obtaining informed consent, and ensuring confidentiality of the study information.

Inclusion criteria:

- Age ≥ 18 years
- Patients with chronic liver disease evidenced by clinical, biochemical &ultrasonographic evidences
- Patients who gave informed written consent

Exclusion criteria:

- Patients with acute liver failure and hepatocellular carcinoma
- Patients with severe life-threatening infection and acute emergency condition
- Patients who had any secondary cause associated with osteoporosis

- Patients with chronic kidney disease, diabetes mellitus, history of endocrine disease, metastatic bone disease or other malignancies

III. RESULTS

Table 1: Demographic profile of the study subjects (N=60).

Variable	CLD (n=30)	Comparison group (n=30)	p-value
Age (years)			
≤30	2 (6.7)	11 (36.7)	
31 – 40	6 (20.0)	9 (30.0)	
41 – 50	8 (26.7)	5 (16.7)	<0.001
>50	14 (46.7)	5 (16.7)	
Mean ± SD	49.76 ± 12.02	37.96 ± 12.35	
Gender			
Male	21 (70.0)	14 (46.7)	
Female	9 (30.0)	16 (53.3)	0.042

*Unpaired t test and Chi-Square test was done to measure the level of significance

Table 1 shows among 30 patients with chronic liver disease (CLD), 21 (70%) were males and 9 (30%) were females. The minimum age of the patients was 18 years and the maximum was 70 years, with mean age of 49.76 (± SD, ± 12.02) years which is statistically significant (p-value= <0.001).

Table 2: Biochemical findings (N=60).

Variable	CLD (n=30)	Comparison group (n=30)	p-value
Serum albumin (g/dl)	2.83 ± 0.60	4.03 ± 0.23	<0.001
Serum calcium (mg/dl)	8.05 ± 0.76	8.81 ± 0.49	<0.001
Serum creatinine (mg/dl)	1.05 ± 0.36	0.81 ± 0.16	0.001
Serum bilirubin (mg/dl)	2.09 ± 1.82		
Prothombin time (sec)	15.74 ± 2.45		
INR	1.33 ± 0.21		
Platelet (/cmm)	135233 ± 74483	325000±35355	0.001

* Unpaired t test was done to measure the level of significance

Table 2 shows distribution of some baseline variables among the study group. It was observed that serum albumin, serum calcium levels and platelet count were significantly lower among patient with CLD in comparison to healthy individuals (p= <0.05).

Table 3: Serum 25(OH)D level in patients with CLD and healthy individuals (N=60).

Serum 25(OH)D level	CLD (n=30)	Comparison group (n=30)	p-value
Deficient	19 (63.4)	7 (23.3)	0.007
Insufficient	10 (33.3)	20 (66.7)	
Sufficient	1 (3.3)	3 (10.0)	

*Chi-Square test was done to measure the level of significance

Table 3 reflected that many patients with chronic liver disease had either deficient or insufficient vitamin D levels. Patients were categorized into three groups according to vitamin D levels: patients with deficient (<20 ng/mL), insufficient (20–30 ng/mL) and sufficient (>30 ng/mL) vitamin D levels. The majority of patients with chronic liver disease (n = 19) had deficient vitamin D levels (patients: 63.3% vs. comparison group: 23.3%). This difference was statistically significant (p value = 0.007). Sufficient levels of vitamin D were found in only 1 patient with chronic liver disease (patients: 3.3% vs. comparison group: 10%).

Table 4: Serum calcium level in patients with CLD and healthy individuals (N=60)

Serum Calcium	CLD (n=30)	Comparison group (n=30)	p-value
Low	25 (83.3)	4 (13.3)	<0.001
Normal	5 (16.7)	26 (86.7)	

Chi-Square test was done to measure the level of significance

Table 4 shows serum calcium level in patient with CLD and healthy individual. Serum calcium level was significantly lower in patient with CLD than the healthy individual (patients: 8.05 ± 0.76 mg/dl vs. comparison groups: 8.81 ± 0.49 mg/dl; p value = <0.001).

Table 5: Association of serum 25(OH) D level with CTP class of cirrhosis of the liver (n=30).

Variable	CTP-A (n=9)	CTP-B (n=12)	CTP-C (n=9)	p-value
Deficient	2 (22.2)	11 (91.7)	6 (66.7)	0.021
Insufficient	6 (66.7)	1 (8.3)	3 (33.3)	
Sufficient	1 (11.1)	0 (0.0)	0 (0.0)	

Table 5 shows association of serum 25(OH)D level with Child-Turcotte-Pugh (CTP) class of cirrhosis of the liver. Most patients with CTP class C were vitamin D deficient, while none had sufficient vitamin D stores. In contrast to this, 2 (22.2%) patients having CTP class A had deficient vitamin D levels. The results indicated that vitamin D levels in cirrhotic patients are associated with CTP classification (p <0.05). Vitamin D levels were strongly related to CTP classification of liver cirrhosis.

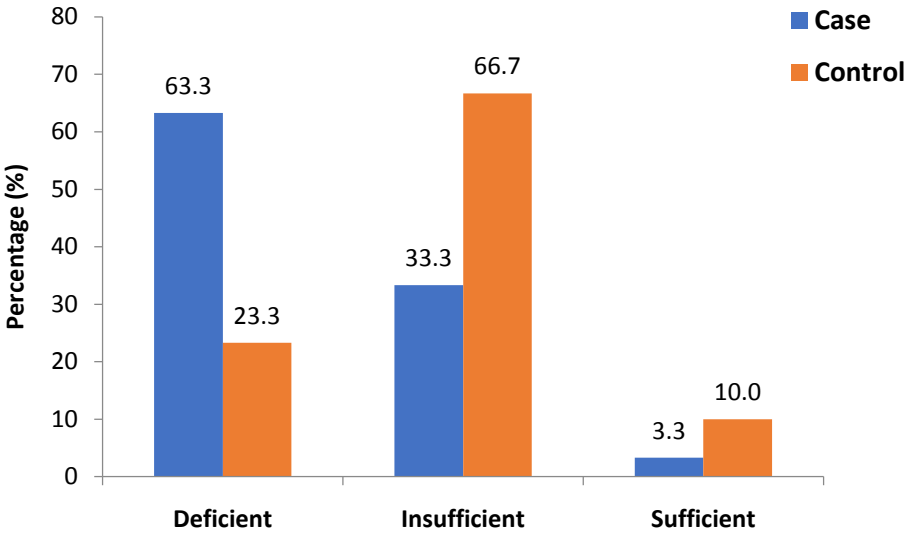

Figure 1: Patients with chronic liver disease and controls according to vitamin D categories

Figure 1 presents three categories of vitamin D levels in the patients and comparison groups in the bar diagram. Three categories of vitamin D levels are: deficient, insufficient and sufficient. Vitamin D deficiency was much higher in patient with CLD than healthy individuals. But, healthy individuals were also insufficient in vitamin D level.

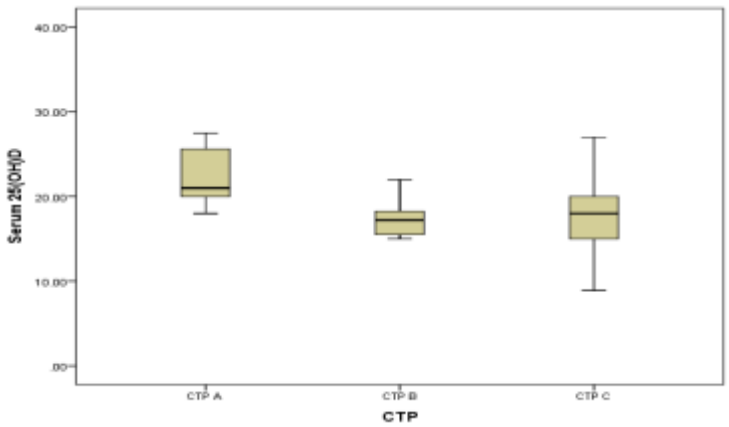

Figure 2: Serum 25(OH)D levels in different CTP classes of patients with chronic liver disease

Fig. 2 shows serum 25(OH) D levels in different Child-Turcotte-Pugh classes of patients with chronic liver disease. It shows relatively higher serum vitamin D in patient with CTP class A than CTP class B and CTP class C. This indicates as the CTP class advances, vitamin D levels decrease.

IV. DISCUSSION

This observational cross-sectional study was conducted in the department of Gastroenterology, BSMMU, Dhaka with an objective to assess level of serum vitamin D and calcium among patients. In this study we enrolled thirty (30) patients with chronic liver disease who were admitted in department of Gastroenterology, BSMMU. We also included thirty (30) healthy persons attending the department of Gastroenterology, BSMMU along with patients.In this study patients with CLD had a significantly higher mean age compared to the comparison group (49.76 years vs. 37.96 years, $p < 0.001$). This finding suggests that CLD tends to affect individuals at an older age, which aligns with previous studies reporting an increased prevalence of liver diseases in the elderly population [14]. Additionally, a higher proportion of males were observed in the CLD group compared to females (70% vs. 30%, $p = 0.042$), indicating a potential gender disparity in the prevalence of CLD.In this study CLD group exhibited significantly lower levels of serum albumin, serum calcium, and platelet count compared to the healthy individuals ($p < 0.05$). These findings are consistent with previous similar research documenting the impact of CLD on liver function, calcium metabolism, and platelet count which were found significantly lower levels(($p < 0.05$)) [10], [15]. Reduced serum albumin levels in CLD patients indicate impaired liver synthetic function, while lower serum calcium levels may be attributed to liver dysfunction affecting vitamin D metabolism and calcium homeostasis. The decreased platelet count suggests liver dysfunction-related thrombocytopenia, which is a common feature in CLD [16].In this study a significant association between CLD and vitamin D deficiency. The majority of CLD patients (63.4%) had deficient vitamin D levels, while only a small proportion (3.3%) had sufficient levels. Another study found (92.4%) deficient vitamin D levels [17]. More previous studies indicating a high prevalence of vitamin D deficiency in patients with CLD [18], [19]. The liver plays a crucial role in vitamin D metabolism, and impaired liver function can lead to decreased synthesis and impaired conversion of vitamin D precursors. Vitamin D deficiency in CLD patients has significant clinical implications, as it may contribute to the progression of liver disease and exacerbate the risk of complications.In this study the association between vitamin D levels and the Child-Turcotte-Pugh (CTP) class of cirrhosis results demonstrate that vitamin D deficiency was more prevalent in patients with advanced CTP class C (66.7%) compared to class B (91.7%) and class A (22.2%). This association between vitamin D deficiency and cirrhosis severity suggests that vitamin D status could serve as a potential prognostic marker for assessing the progression of liver disease. Similar findings have been reported in previous studies, supporting the hypothesis that vitamin D deficiency may contribute to the pathogenesis and severity of liver cirrhosis [20], [21].In this study comparing the findings of this study with previous research, several similarities and differences emerge. The prevalence of vitamin D deficiency in CLD patients aligns with existing literature, which consistently reports high rates of deficiency in this population [22], [23]. Similarly, the lower levels of serum albumin and platelet count observed in CLD patients are consistent with established liver disease pathophysiology [24]. However, the difference in serum calcium levels between CLD patients and healthy individuals appears to be more pronounced in this study compared to some previous reports [10], [25]. These discrepancies could be attributed to variations in sample sizes, patient characteristics, or assay methods employed in different studies.

V. LIMITATIONS OF THE STUDY

The study is the relatively small sample size, which may limit the generalizability of the findings.

VI. CONCLUSION

In summary, this study found that chronic liver disease (CLD) is associated with older age, male predominance, lower levels of serum albumin, calcium, and platelet count, as well as a high prevalence of vitamin D deficiency. However, the small sample size limits the generalizability of the findings.

VII. RECOMMENDATION

A further multi-centric case-control study with large sample size might be carried out to find out associated causes of vitamin D deficiency and low serum calcium in patients with chronic liver disease. A randomized controlled trial can be done to observe effect of vitamin D supplement in patients with CLD. Vitamin D levels can be routinely checked in every patient suffering from advanced CLD. Finally, vitamin D supplement might be an adjunct to improve the patient's quality of life in patients with CLD.

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