

## ORIGINAL ARTICLE

**Vitamin D Deficiency in Patients with Chronic Liver Disease: A Clinical Study at A Tertiary Care Hospital**ISLAM SHAH<sup>1</sup>, WIQAS AHMAD<sup>2</sup>, FAROOQUE ISLAM<sup>3</sup>, MUHAMMAD HANIF HADI<sup>4</sup>, JAWAD MAHMOOD<sup>5</sup>, MUHAMMAD KASHIF<sup>6</sup><sup>1</sup>Senior Registrar of Medicine, Timergara Medical College, and Teaching Hospital<sup>2</sup>Specialist Registrar Gastroenterology, MTI Hayatabad Medical Complex Peshawar<sup>3</sup>Trainee Medical Officer Gastroenterology, MTI Hayatabad Medical Complex Peshawar<sup>4</sup>Registrar Gastroenterology, MTI Bacha Khan Medical Complex Swabi<sup>5</sup>International Trainee Fellow, Good Hope Hospital, University Hospital Birmingham, NHS Trust UK<sup>6</sup>Trainee Medical Officer Gastroenterology, MTI Lady Reading Hospital PeshawarCorresponding author: Wiqas Ahmad, Email: [wiqasahmad642@gmail.com](mailto:wiqasahmad642@gmail.com)**ABSTRACT**

**Background:** Patients with chronic liver disease (CLD) have deficiencies of multiple nutrients and compare to other nutrients vitamin D deficiency occurs more commonly in patients with CLD. Due to liver fibrosis, synthetic functions of the liver are reduced, leading to vitamin D deficiency through impaired activation via a reduction in vitamin D Binding Protein. Reduction in performance status and dietary deficiency further adds to the scenario. The study assessed the frequency of vitamin D deficiency in chronic liver disease patients and its association with the severity of chronic liver disease.

**Methodology:** The department of gastroenterology at the Hayatabad Medical Complex in Peshawar carried out this descriptive study. 141 CLD patients who satisfied the criteria were included in the research. Three groups of patients were divided based on their Child-Pugh scores. The patient's vitamin D levels were examined by hospital laboratories. Serum (25,OH)D concentrations below 30 nmol/L were considered to represent [vitamin D] insufficiency levels. The data were examined using SPSS version 22.

**Results:** 141 CLD patients were assessed. In this study the (mean age) was  $53.40 \pm 12.194$  years. The (male-to-female ratio) was 2.4:1. Hepatitis C was the underlying etiology in 56.7% of CLD patients. 83 patients (58.9%) had Child-Pugh Class C chronic liver disease. Ninety-five patients (67.4%) had low vitamin D levels. Vitamin D insufficiency correlated with gender and (Child-Pugh Class)

**Conclusion:** Patients with liver cirrhosis are frequently vitamin D deficient. In our study, 67.4% patients were found to have deficient vitamin D levels. Vitamin D deficiency was more common in females and those with advanced liver fibrosis.

**Keywords:** Vitamin D deficiency, Vitamin D level, Fibrosis, Chronic liver disease (CLD)

**INTRODUCTION**

Chronic liver disease (CLD) is a multi-nutrient deficient state. Patients with CLD are susceptible to micro and macronutrient deficiency ranging from protein and several vitamin deficiencies to minerals like zinc and selenium. (Deficiency of fat-soluble vitamins) is also frequently observed<sup>01</sup>. Vitamin D insufficiency is frequent in severe chronic liver disease patients, although people with less severe chronic liver disease may also be deficient<sup>02</sup>. Vitamin D deficiency increases mortality, morbidity, and CLD consequences such as recurring bacterial infections and portal hypertension problems<sup>03</sup>. CLD disease patients may have low vitamin D due to hepatic vitamin D metabolism alteration<sup>04</sup>. Under UV radiation, the skin synthesizes inactive vitamins D<sub>2</sub> and D<sub>3</sub>, which the liver activates by hydroxylation. In liver fibrosis, the liver loses its capacity to hydroxylate the inactive form of vitamin D and consequently patients with Child-Pugh Class C have significant frequency of low vitamin D levels<sup>05</sup>. Vitamin-D deficient diet, decreased vitamin- D intestinal absorption, and sunshine reduction worsen the situation<sup>06</sup>. Vitamin D deficiency in chronic liver disease patients varies with fibrosis severity. Falak et al. found 55.2% vitamin D insufficiency in decompensated cirrhotic patients and 13.6% in compensated ones<sup>07</sup>. Arteh et al. found 92% of chronic liver disease patients had vitamin D insufficiency, with a preponderance of Afro-American race. Our country has few studies regarding vitamin D insufficiency in chronic liver disease patients, and its relationship with liver disease status. This research addresses this information gap<sup>08</sup>.

**METHODOLOGY**

The institution's ethical review board gave its clearance for this study, which was carried out in the gastroenterology unit of the Hayatabad Medical Complex from December 2022 to August 2023.

**Inclusion Criteria:** CLD patients from 20 to 80 years and of both genders fulfilling the study criteria were included. CLD was diagnosed if patients had one or more of the following: (1) If they have biochemical and synthetic function abnormalities suggestive of CLD along with risk factors for CLD. (2) Features of CLD such as

surface nodularity, coarse heterogeneous echotexture, hypertrophic or atrophic liver segments on ultrasound<sup>09</sup>. (3) Liver biopsy or medical records suggested CLD. Child-Pugh scores divided CLD patients into three groups. Patients with a Child-Pugh score of six or less were categorized as Class A, seven to nine as Class B, and higher than nine as Class C.

**Exclusion Criteria:** Patients with a history of vitamin-D deficiency, chronic renal illness, vitamin- D supplementation, and steroid use in the last six months were excluded.

**Data Collection:** Demographics including age, gender, the underlying cause of CLD, duration of CLD, and Child-Pugh Class were noted from patients' records. Relevant history of vitamin D deficiency like bone fractures was taken, followed by detailed physical examination for any signs of hypovitaminosis D. Vitamin D level was determined in the hospital laboratory in the blood sample of the patient. Serum vitamin D 25,OH, D levels below 30 nmol/L are considered inadequate.

**Data Analysis:** IBM SPSS 22 statistical program analyzed the data. For qualitative variables such as gender, CLD etiology, Child-Pugh Class, and low vitamin D levels, frequencies and percentages were computed. Mean  $\pm$  SD were calculated for quantitative variable such as Age, CLD duration, and blood vitamin D levels. To determine statistical significance, Chi-Square testing for categorical variables and Student T-tests for continuous variables were also utilized. For the correlation of vitamin D insufficiency with gender, age groups, and Child-Pugh Class, the Chi-Square test of independence with Cramer V nominal was used. Statistics were deemed significant at p-values under 0.05.

**RESULTS**

141 patients included in this study. The mean patient age was  $53.40 \pm 12.194$  years. Range of patient's age was between 20 to 80 years. Ninety-nine patients (70.2%) were men, and 42 (29.8%) were women. The male-female ratio was 2.4: 1. Table 1 highlights patient features.

Eighty-three patients (58.9%) had Child-Pugh Class C chronic liver disease, and 29 (20.6%) had both Class A and B. HCV was the most prevalent underlying cause of CLD (80 patients, 56.7%), followed by HBV in 31 (22%), HBV+HCV in 11 (7.8%),

PBC in 5 (3.5%), and hemochromatosis ,NAFLD, Wilson or no underlying cause in 14 (9.9%) individuals despite extensive workup. The etiology of these 14 patients was labelled as Miscellaneous. Ninety-five individuals (67.4%) had vitamin D insufficiency. 75 (53.2%) of 141 patients were aged 41-60, and 49 (51.6%) were vitamin D deficient. This study found no age-related vitamin insufficiency correlation ( $p = 0.818$ ). Gender correlated with vitamin D insufficiency ( $p = 0.025$ ). Sixty-one men and 34 women were vitamin D deficient. Vitamin D insufficiency associated with Child-Pugh Class [ $p < 0.001$ ]. (Child-Pugh Class) illness patients have more significant vitamin D insufficiency. 76 of 83 Child Class patients were vitamin D deficient.

Table 1: characteristics and percentage n-141

[Characteristics ]	[N] (%)
1.Age (Years)	
2.Mean	53.40
3.Standard Deviation	12.194
4.Range	20-80
5.Gender	
6..Male	99 (70.21)
7.Female	42 (29.79)
8.Etiology Of CLD	
9.Hepatitis C	80 (56.74)
10.Hepatitis B	31 (21.98)
11.Hepatitis C And Hepatitis B	11 (7.80)
12.Primary Biliary Cirrhosis	05 (3.55)
13.Miscellaneous	14 (9.93)

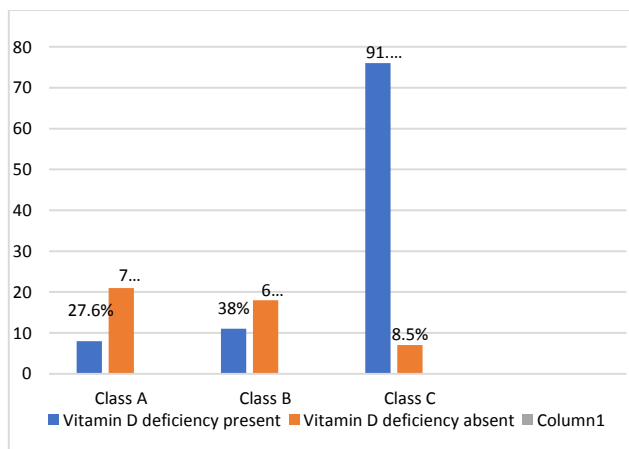


Figure 1: Vitamin D Deficiency in Various Classes of Child-Pugh Class

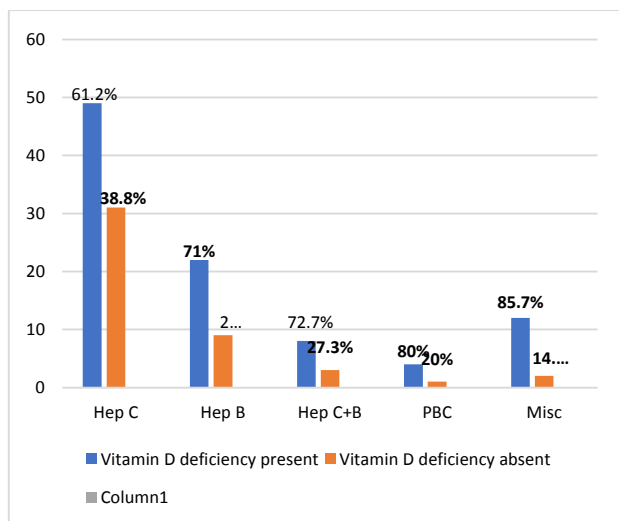


Figure 2: Vitamin D Deficiency Status Based on Etiology of CLD

## DISCUSSION

The body's vitamin D requirement is fulfilled by absorption through the gut from dietary sources. Secondly, it is also predominantly synthesized endogenously in the skin's epidermal cells through exposure to ultraviolet radiation<sup>10</sup>. The inactive vitamin D thus synthesized is subjected to the liver for activation through hydroxylation via a protein called vitamin D binding protein (DBP), an analog of albumin. In fibrotic diseases like chronic liver disease (CLD), where the normal parenchyma of the liver is replaced with fibrous tissue, the synthetic function of the liver is compromised, leading to reduction of DBP, which eventually leads to vitamin D deficiency<sup>11</sup>.

67.4% of CLD patients were vitamin D deficient in this study. Arteh et al. found 92.4% of vitamin D deficiency in their research. Similarly, 76.5% of patients had vitamin D insufficiency in the study conducted by Falak et al. These studies may have a high vitamin D insufficiency rate since more women than men participated. In general, gender affects vitamin D insufficiency, and chronic liver disease patients are no exception. Johnson and colleagues found that female with CLD are increased risk for vitamin D deficiency<sup>12</sup>. According to the data we collected, vitamin D deficiency is more prevalent among females. with CLD than in men ( $p < 0.025$ ). Our local population eat mostly protein, which may contribute to dietary deficiency of vitamin D. Due to religious and socio-cultural beliefs, women are less exposed to sunshine, which also causes vitamin D insufficiency. Vitamin D insufficiency inversely correlated with patient Child-Pugh scores ( $p < 0.001$ ). As fibrosis progressed from Class A and B to C, the deficit of vitamin D increased. As fibrosis progresses, liver synthesis function decreases, reducing DBP, which activates vitamin D. The Jamil et al. investigation found similar tendencies<sup>13</sup>.

## CONCLUSION

Most of the patients with CLD have low vitamin D levels. Vitamin D insufficiency is more common in women and those who have severe fibrosis. To evaluate vitamin D insufficiency in CLD patients in our community, large-scale multicenter studies should be done. Vitamin D levels should be checked in all patients with CLD and promptly treated if found deficient

## REFERENCES

- Zaina FE, Parolin MB, Lopes RW, Coelho JC. Prevalence of malnutrition in liver transplant candidates. *Transplant Proc.* 2004;36(4):923-5.
- Fisher L, Fisher A. Vitamin D and parathyroid hormone in outpatients with non cholestatic chronic liver disease. *Clin Gastroenterol Hepatol.* 2007;5(4):513-20.
- Zittermann A, Iodice S, Pilz S, Grant WB, Bagnardi V, Gandini S. Vitamin D deficiency and mortality risk in the general population: a meta-analysis of prospective cohort studies. *Am J Clin Nutr.* 2012;95(1):91-100.
- Anty R, Tonohouan M, Ferrari-Panaia P, Piche T, Pariente A, Anstee QM, et al. Low Levels of 25-Hydroxy Vitamin D are Independently Associated with the Risk of Bacterial Infection in Cirrhotic Patients. *Clin Transl Gastroenterol.* 2014;5(5):e56.
- Arteh J, Narra S, Nair S. Prevalence of vitamin D deficiency in chronic liver disease. *Dig Dis Sci.* 2010;55(9):2624-8.
- Heuman DM, Mihas AA, Habib A, Gilles HS, Stravitz RT, Sanyal AJ, et al. MELD-XI: a rational approach to "sickest first" liver transplantation in cirrhotic patients requiring anticoagulant therapy. *Liver Transplant.* 2007;13(1):30-7.
- Stokes CS, Volmer DA, Grünhage F, Lammert F. Vitamin D in chronic liver disease. *Liver Int.* 2013;33(3):338-52.
- Falak S, Aftab L, Saeed M, Islam A. Prevalence of Vitamin-D deficiency is related to the severity of liver damage in Hepatitis-C patients. *Pak J Med Sci.* 2020;36.
- Jamil Z, Arif S, Khan A, Durrani AA, Yaqoob N. Vitamin D Deficiency and Its Relationship with Child-Pugh Class in Patients with Chronic Liver Disease. *J Clin Transl Hepatol.* 2018;6(2):135-40.
- Zhang R, Naughton DP. Vitamin D in health and disease: Current perspectives. *Nutr J.* 2010;9(1):65.
- Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. *Ann Gastroenterol.* 2016;29(3):297-306.
- Johnson LK, Hofsoe D, Aasheim ET, Tanbo T, Holven KB, Andersen LF, et al. Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study. *Eur J Clin Nutr.* 2012;66(1):83-90.
- Khaghani S, Narjes A, Pasalar P, Sedegh S, Nowrouzi A, Samira H. Effect of Progesterone-only Contraception on Vitamin D in Human Milk. *Iranian Journal of Pediatrics.* 2008;18.