Original Article

Vitamin D Deficiency in Patients with Chronic Liver Disease

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ABSTRACT

Objective: To find the frequency of vitamin D deficiency in patients with chronic liver disease and evaluate the relationship of vitamin D deficiency with advancement in liver disease severity.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Lady Reading Hospital, Peshawar from August 2020 to February 2021.

Materials and Methods: One hundred and forty one patients with chronic liver disease were enrolled. Vitamin D level was measured in the blood sample of patients in the hospital laboratory. The cut-off value for vitamin D deficiency was set at Serum vitamin D [25 (OH) D] level <30 nmol/L.

Results: Ninety nine patients (70.2%) were males and 42 patients (29.8%) were females. The mean age was 53.40±12.19 years. Hepatitis C was the most common underlying cause of chronic liver disease observed in 80 patients (56.7%). 83 patients (58.9%) had Child-Pugh Class C chronic liver disease. Vitamin D deficiency was observed in 95 patients (67.4%). Gender and Child-Pugh Class had a significant association with vitamin D deficiency.

Conclusion: Vitamin D deficiency is a frequently occurring finding in patients. Female patients with advanced liver fibrosis are more likely to have vitamin D deficiency.

Key Words: Vitamin D deficiency, Fibrosis, End stage liver disease

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INTRODUCTION

Chronic liver disease is a multi-nutrient deficiency condition. Patients with Chronic liver disease 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.[1] Vitamin D is one of the fat-soluble vitamins. Though deficiency of vitamin D is fairly common in advanced chronic liver disease, patients with a milder form of liver illness are also susceptible to a certain extent of vitamin D inadequacy.[2] Vitamin D deficiency has implications in terms of increased risk of mortality, morbidities, and precipitation of Chronic liver disease related complications, including recurrent bacterial infections and portal hypertensive complications.[3,4]

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The low level of vitamin D in chronic liver disease patients may be attributed to an imbalance in vitamin D metabolism in the liver. Synthesized in an inactive form (vitamin D2 and D3) in the skin under the effect of UV light, the inactive vitamin D is subjected to activation through hydroxylation in the liver. In liver fibrosis, the liver loses its ability to hydroxylase the inactive form of vitamin D leading to deficiency of active vitamin D, which is evident from the fact that the deficiency is more common in patients with Child-Pugh Class C liver disease.[5,6] Decreased dietary vitamin D, decreased intestinal absorption, and decreased exposure to sunlight further aggravate the condition of the patient[7]. Depending upon the severity of fibrosis, there are different reports about the prevalence of vitamin D deficiency in patients with chronic liver disease. There is lack of data about vitamin D deficiency in chronic liver disease patients in our country with respect to its prevalence and its association with disease severity.

The main aim of this study is to know the prevalence of vitamin D deficiency in chronic liver disease in our local set up so that to design strategies to prevent and treat vitamin D deficiency in patients suffering from chronic Liver disease.

MATERIALS AND METHODS

This descriptive study was conducted at the Department of Gastroenterology, Lady Reading Hospital Peshawar after approval from the ethical review board from 20th August 2020 to 20th February 2021. Patients in the age

range of 20 to 80, both genders with chronic liver disease (CLD) were included. Patients with a history of vitamin D deficiency prior to CLD, patients with a history of chronic kidney disease, vitamin D supplements, and steroid intake in the last six months were excluded. Patients were labeled as having CLD if they had one or more of the following features: (1) If they have biochemical abnormalities suggestive of CLD like deranged liver and synthetic functions and risk factors leading to CLD. (2) Sonographic features of CLD like surface nodularity, coarse heterogeneous echotexture, hypertrophic or atrophic liver segments.[9] (3) Liver biopsy findings of CLD or medical records were suggestive of CLD. Patients with CLD were classified into three classes based on their Child-Pugh score. Patients with a Child-Pugh score of six or less than six were classified as Child-Pugh Class A, those with a score of seven to nine as Child-Pugh Class B, and patients with a score of greater than nine were classified as Child-Pugh Class C. Patients with a history of vitamin D deficiency prior to CLD, patients with chronic kidney disease, vitamin D supplements, and steroid intake 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 vitamin D deficiency. Vitamin D level was determined in the hospital laboratory in the blood sample of the patient. Serum vitamin D [25(OH) D] levels less than 30nmol/L were labelled as deficient vitamin D. Analysis of the data was performed using SPSS-22.

RESULTS

There were 99 (70.2%) males and 42 (29.8%) were females. The male to female ratio was 2.4:1 (Table 1). The patient's age ranged from 20 to 80 years, while the mean age of the patients was 53.40±12.194 years. Majority of patients were in the age range of 46 to 60 (Table 2). Eighty three patients (58.9%) had Child-Pugh Class C chronic liver disease, while both Child-Pugh Class A and B were present in 29 (20.6%) patients each (Table 3). The most common underlying cause of CLD was chronic hepatitis C in 80 (56.7%), followed by chronic hepatitis B in 31 (22%), hepatitis B and hepatitis C co-infection in 11 (7.8%), PBC in 5 (3.5%) patients while in 14 patients (9.9%) patients, the underlying cause was either autoimmune hepatitis, non-alcoholic fatty liver, Wilson disease, hemochromatosis or the cause was unknown despite workup. The aetiology of these 14 patients was labelled as "miscellaneous" in this study (Table 4). Vitamin D deficiency was observed in 95 (67.4%) patients, 61 (64.21%) male and 34 (35.78%) female patients. Vitamin D deficiency was more common in patients with Child-Pugh Class C disease. Out of 83 Child Pugh Class C patients, 76 (91.56%), 11 (37.93%) child Pugh class B and 8 (27.58%) child Pugh class A chronic liver disease patients were having vitamin D deficiency (Table 5).

Table No.1: Frequency of genders (n=141)

Gender	No	%
Male	99	70.21
Female	42	29.79

Table No.2: Frequency of age (n=141)

Age	No.	%
20-30	21	14.89
31-45	40	28.36
46-60	80	56.73
61-80	20	14.18
Mean±SD	53.40±12.19	

Table No.3: Child class wise distribution of patients

Child class	No.	%
Child A	29	20.60
Child B	29	20.60
Child C	83	58.90

Table No.4: Aetiology wise distribution of chronic liver disease patients

Aetiology	**No.**	**%**
Hepatitis C	80	56.74
Hepatitis B	31	21.98
Hep B and C co-infection	11	7.80
Primary biliary cirrhosis	5	3.55
Miscellaneous	14	9.93

Table No.5: Vitamin D deficiency wise distribution of patients

Child class	**No.**	**%**
Child-A	8	27.58
Child-B	11	37.93
Child -C	76	91.56

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.[8] The inactive vitamin D thus synthesized is subjected to the liver for activation through hydroxylation via a protein called vitamin D binding protein (DBP) and an analog of albumin. In fibrotic diseases like chronic liver disease, 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.[9]

Our study showed high prevalence 76 (91.56%) of vitamin- D deficiency in cirrhotic patients of various aetiologies. These results of our study are almost

similar to the study done by Arteh et al[5] in USA where 118 patients were studied and there was 92.4% prevalence of vitamin D deficiency in their patients.
Similarly the results of our study are also comparable to the study done Jamil et al[10] in Rawalpindi where total of 125 were studied and 88% had vitamin D deficiency. However the results of our study are somewhat different from the study done by Falak et al[11] in Faisalabad where vitamin D deficiency was reported in 76.5% of patients .The female gender and advanced chronic disease patients were more sufferer of vitamin-D deficiency in our study and same results were reported by Johnson and colleagues[12] in their study as well. Adults in our local population primarily consume proteinaceous diets, which may lead to dietary factors of deficiency as well. Moreover, females are less exposed to sunlight due to religious and socio-cultural concepts, which is also proven to lead to vitamin D deficiency.[13] Association of vitamin D deficiency was observed with the Child-Pugh score of the patients in inverse fashion. Vitamin D deficiency was more frequently observed as the patient's fibrosis score progressed from Class A and B to C. This effect could be explained due to reduction in the synthetic function of the liver, which is decreased as the fibrosis advances, eventually leading to reduction of DBP, which is necessary for activation of vitamin D. These results are in conformity with the results of the study conducted by Jamil et al.[10].

CONCLUSION

Vitamin D deficiency is a frequent finding in patients with chronic liver disease. Female patients and those with advanced fibrosis are more likely to have vitamin D deficiency.

Author's Contribution:

Concept & Design of Study:	Dilaram Khan
Drafting:	Fakhare Alam, Jan Dil Khan
Data Analysis:	Jan Dil Khan, Fakhare Alam
Revisiting Critically:	Dilaram Khan, Fakhare Alam
Final Approval of version:	Dilaram Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Zaina FE, Parolin MB, Lopes RW, Coelho JC. Prevalence of malnutrition in liver transplant candidates. Transplant Proc 2004;36(4):923-5.
2. Fisher L, Fisher A. Vitamin D and parathyroid hormone in outpatients with noncholestatic chronic liver disease. Clin Gastroenterol Hepatol 2007;5(4):513-20.
3. 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.
4. 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.
5. Arteh J, Narra S, Nair S. Prevalence of vitamin D deficiency in chronic liver disease. Dig Dis Sci 2010;55(9):2624-8.
6. 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 Transpl 2007; 13(1):30-7.
7. Stokes CS, Volmer DA, Grünhage F, Lammert F. Vitamin D in chronic liver disease. Liver Int 2013;33(3):338-52.
8. Zhang R, Naughton DP. Vitamin D in health and disease: current perspectives. Nutr J 2010; 9:65.
9. Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. Ann Gastroenterol 2016; 29(3):297-306.
10. 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.
11. Falak S, Aftab L, Saeed M, Islam A. Prevalence of Vitamin-D deficiency is related to severity of liver damage in Hepatitis-C patients. Pak J Med Sci 2020;36(3):445-50.
12. Johnson LK, Hofsø 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.
13. Zargar AH, Ahmad S, Masoodi SR, Wani AI, Bashir MI, Laway BA, et al. Vitamin D status in apparently healthy adults in Kashmir Valley of Indian subcontinent. Postgrad Med J 2007; 83(985):713-6.