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ORIGINAL ARTICLE

Prevalence and Impact of Vitamin D Deficiency Among Individuals Diagnosed with Chronic Liver Disease

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ABSTRACT

Introduction: Chronic liver disease is characterized by multi-nutrient deficiency. The propensity for individuals to have vitamin D insufficiency is greater in comparison to other essential minerals. Fibrosis results in a decline in the liver's ability to perform synthetic functions ultimately leading to lack of vitamin D due to poor activation caused by drop in proteins binding the vitamin. The situation is exacerbated by the decrease in productivity and the presence of nutritional deficiencies.

Materials and Methods: The present descriptive research was carried out in the Department of Medicine at DHQ Teaching Hospital Haripur spanning from 1st January 2022 to 31st December 2022. The study population consisted of individuals between the ages of 40 and 70 years who were diagnosed with chronic liver disease. The concentration of vitamin D was assessed in blood samples obtained from patients at the hospital laboratory. The established threshold for identifying vitamin D insufficiency is a blood vitamin D level below 30 nmol/L. Data analysis was performed using statistical software SPSS version 24.

Results: The age of the patients ranged from 40 to 70 years. The mean age of the patients was 53.40 years with standard deviation 12.194. Age wise distribution revealed 60.1% patients (n = 89) in the age group 40-55 years and 39.9% participants (n = 59) had age 56-70 years. The number of male participants were 94 (63.5%). Vitamin deficiency was observed in 64.9% patients (n = 96). The association of vitamin D deficiency with disease duration, child class and gender were statistically significant ($p < 0.05$).

Conclusion: The potential association between vitamin D insufficiency and the extent of liver function impairment, degree of fibrosis, and susceptibility to infection consequences suggests that it may serve as a valuable prognostic indicator and diagnostic tool. Additional research is required to thoroughly assess and substantiate the significance of vitamin D in the context of liver cirrhosis. This necessitates the undertaking of extensive prospective cohort studies and randomized trials.

Keywords: Vitamin D deficiency, Chronic Liver Disease (CLD)

INTRODUCTION

Chronic liver disease is characterized by deficiency of several nutrients. Individuals diagnosed with chronic liver disease are prone to experience deficiencies of both micro and macro nutrients. These deficiencies may include a range of essential substances, including proteins, various vitamins, as well as minerals such as zinc and selenium. The occurrence of insufficiency of fat-soluble vitamins is also often noticed.[1,2]

One of the vitamins that are soluble in fat is vitamin D. Patients with even milder form of liver sickness are vulnerable to have some extent of vitamin D insufficiency, despite the fact that vitamin D deficiency is more frequent in severe chronic liver disease.[3] Vitamin D deficiency is associated with an increased risk of mortality, morbidities, and the precipitation of CLD-related problems such as recurrent bacterial infections and portal hypertension complications. These risks may be mitigated by adequate supplementation with vitamin D.[4]

There is a possibility that an imbalance in the vitamin D metabolism in the liver is accountable for the low levels of vitamin D seen in people with chronic liver disease. Under the influence of ultraviolet radiation, vitamin D is produced in the skin in an inert state (vitamin D2 and D3). This form of vitamin D is then transported to the liver, where it is activated by a process called hydroxylation.[5] As a result of liver fibrosis, the liver reduces its capacity to hydroxylase the inactive form of vitamin D, which results in lack of active vitamin D. This deficiency is more prevalent in individuals who have Child Pugh Class C liver disease, as can be shown by the fact that people with this kind of liver disease are more likely to have the condition.[6] The situation is made even worse by a lower amount of vitamin D in the food, a decreased amount of intestinal absorption, and a decreased amount of exposure to sunshine.[7]

The link between vitamin D blood concentration and the severity of liver disease has been controversially studied in the past, with conflicting findings. However, other research has failed to discover any significant variation in vitamin D levels between cirrhotic and noncirrhotic patients, or between different Child-Pugh groups.[8] Vitamin D insufficiency in alcoholics and those with cholestatic liver disease has received much of the attention. So, we set out to see how common vitamin D insufficiency is and how it relates to the degree of liver dysfunction among people who have chronic liver disease of diverse etiologies. This is true both in terms of the severity of the illness and the cause of it. This information gap is one that the authors of this research want to fill with their findings.

MATERIALS AND METHODS

Setting: This descriptive study was conducted at the Department of Medicine, DHQ Teaching Hospital, Haripur after approval from ethical review board from 1st January 2022 to 31st December 2022.

Population: Male and female patients aged 40 to 70 years who presented with chronic liver disease were considered. Features such as weakness, palmar erythema, jaundice, hair loss, skin bruising, oedema, caput medusae and manifestations of decompensation such as ascites and hepatic encephalopathy were used to consider the diagnosis of chronic liver disease. The diagnosis was confirmed after a series of biochemical and radiographic tests. On ultrasonography, small shrunken liver, portal hypertension, splenomegaly and ascites were indicative of chronic liver disease and liver cirrhosis. Patients having a previous diagnosis of vitamin D deficiency, a history of chronic kidney disease, current or recent use of vitamin D supplements or steroids were dropped out.

Data Collection Procedure: Demographics including age, gender, underlying cause of CLD, duration of CLD and Child Pugh Class were noted from patients' record. 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 patient.

Outcome: Measurement of Serum vitamin D level in blood was the primary end point. Serum vitamin D level less than 30 nmol/L was labelled as deficient vitamin D.

Data Analysis: Statistical software, SPSS version 24, was used to analyze the data. Frequencies and percentages were computed for categorical variables. Means and standard deviations were computed for continuous variables. The Student t test was used to analyze continuous variables, whereas Chi Square tests were used to analyze categorical ones.

RESULTS

The total number of patients with chronic liver disease included in this study was 148. The age of the patients ranged from 40 to 70 years. The mean age of the patients was 53.40 years with standard deviation 12.194. Age wise distribution revealed 60.1% patients (n = 89) in the age group 40-55 years and 39.9% participants (n = 59) had age 56-70 years. The number of male participants was 94 (63.5%) and that of females was 54 (36.5%). The mean BMI of the enrolled candidates was 20.59 kg/m^2 with standard deviation 1.36. The percentage of patients with BMI <20 kg/m^2 was 69 (46.6%) while 79 (53.4%) participants were having more than 20 kg/m^2. Mean ± SD for serum albumin was 2.5 ± 0.71 gm/dl. Child class C cirrhosis was recorded in 76.3% participants (n = 113), Child class B in 18.2% (n = 27) and Child class A cirrhosis was observed in 5.4% patients (n = 08). With respect to etiology, chronic HCV was the most commonly recorded etiology and was registered for 54.7% patients (n = 81), chronic HBV in 31.7% (n = 47), alcoholic cirrhosis in 6.1% (n = 09), PBC was recorded for 4.0% (n = 6) patients and remaining 05 patients (3.4%) had cirrhosis of unknown etiology. The details are listed in table 1.

Table 1: Baseline information and subgroups (n = 148)

Parameters	Subgroups	Frequencies	Percentages
Age (years)	40-55 56-70	89 59	60.1 39.9
Gender	Male Female	94 54	63.5 36.5
BMI (kg/m^2)	≤20 >20	69 79	46.6 53.4
Child Class	A B C	08 27 113	5.4 18.2 76.3
Etiology	HCV HBV Alcoholic PBC Unknown	81 47 09 06 05	54.8 31.7 6.1 4.0 3.4

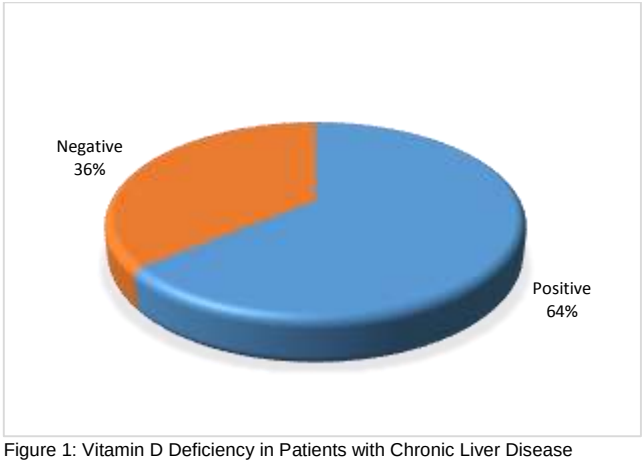

Figure 1: Vitamin D Deficiency in Patients with Chronic Liver Disease

Vitamin D deficiency was found in 96 patients (64.9 %). It was observed in 64.0% (n=57) patients aged 40-55 years versus 66.1% (n = 39) patients aged 56-70 years. The p value for association between presence of vitamin D deficiency and age was 0.672 which was statistically not significant. The number of female patients with vitamin D deficiency was 46 (85.2%) versus 50 (53.2%) in male patients. The p value was <0.001 which was statistically significant. With respect to etiology, 05 (83.3%) out of 06 participants with PBC were positive for vitamin D deficiency. 57 (70.4%) patients out of 81 with chronic HCV were vitamin D deficient.

DISCUSSION

The body's vitamin D needs are met by two primary mechanisms: absorption via the gastrointestinal tract from dietary sources, and predominantly via endogenous synthesis inside the epidermal cells of the skin through exposure to UV radiation. The vitamin D that is synthesized in an inactive form undergoes a process of activation in the liver through hydroxylation, facilitated by a protein known as vitamin D binding protein (DBP), which shares similarities with albumin.[9] Fibrotic illnesses, such as chronic liver disease, include the replacement of the liver's normal parenchyma with fibrous tissue. This fibrotic transformation impairs the synthetic function of the liver, resulting in a decrease in the production of vitamin D-binding protein (DBP) and ultimately leading to vitamin D deficiency.[10]

This study revealed a prevalence rate of 64.9% for vitamin D insufficiency among patients diagnosed with chronic liver disease. However, Arteh et al. documented a prevalence rate of 92.4% for vitamin D insufficiency.[5] In a separate study conducted by Falak et al., it was observed that a significant proportion of patients, specifically 76.5%, exhibited a shortage in vitamin D levels.[8] The elevated prevalence of vitamin D deficiency seen in these studies could potentially be attributed to a higher proportion of female participants in comparison to male patients. The general population and those with chronic liver disease both demonstrate a notable correlation between gender and the occurrence of vitamin D insufficiency. The study conducted by Johnson et al. found a higher prevalence of vitamin D insufficiency among female patients with chronic liver disease.[11] Our study also found a similar tendency ($p < 0.025$), with a higher prevalence of vitamin D deficiency observed in female patients with chronic liver disease (CLD) compared to male patients. Hormonal considerations may contribute to this phenomenon, as female reproductive hormones have been found to have a catabolic effect on vitamin D, whereas male reproductive hormones have been observed to have an anabolic effect on vitamin D.[12] The majority of adults within our local community predominantly adhere to a protein-based diet, which may potentially result in dietary insufficiencies. Furthermore, it has been shown that women have reduced solar exposure because of religious and socio-cultural beliefs, which has been associated with an increased risk of vitamin D insufficiency.[13]

The existing clinical guidelines address the topic of vitamin D supplementation in relation to bone damage in individuals with liver cirrhosis and cholestatic diseases. Nevertheless, there is a contention among certain individuals that the currently defined classifications of vitamin D shortage and insufficiency may not be applicable in the context of patients diagnosed with cirrhosis.[14] It is imperative to establish a more precise delineation of the specifics surrounding vitamin D supplementation. This includes determining the threshold at which supplementation should commence, identifying the optimal duration of supplementation, exploring additional indications for liver-related non-skeletal conditions, customizing dosage for individuals with cirrhosis (maximizing dosages as necessary), determining the optimal level of supplementation, evaluating the method of delivery and bioavailability, establishing appropriate intervals for pre-treatment screening, defining intervals for monitoring efficacy during treatment, and establishing intervals for post-treatment surveillance.[15] In addition, there exist difficulties pertaining to the precision and reliability of the many assays used for measuring 25-hydroxyvitamin D (25(OH)D), which necessitate further investigation and resolution.[16]

A notable correlation was found between vitamin D level and the Child Pugh Score of the patients, exhibiting an inverse relationship. The prevalence of Vitamin D insufficiency increased as the patient's fibrosis score advanced from Class A and B to C. The observed phenomenon may be attributed to a decline in the hepatic synthetic activity, which diminishes as fibrosis progresses. Consequently, this reduction in hepatic function ultimately results in a decrease in the levels of DBP, a crucial component for the activation of vitamin D. This observation aligns with the findings of the study conducted by Jamil et al, which documented comparable patterns.

CONCLUSION

In summary, the association between vitamin D and liver cirrhosis exhibits significant promise for clinical use. In the foreseeable future, it is anticipated that there will be a comprehensive exploration of other signals beyond the skeletal system. The potential correlation between vitamin D insufficiency and liver function, fibrosis severity, and susceptibility to viral consequences suggests that vitamin D levels could serve as a valuable prognostic indicator. Additional research is required to assess and confirm the significance of vitamin D in the context of liver cirrhosis, particularly by the implementation of extensive prospective cohort studies and randomized trials.

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