Burden of Vitamin D Deficiency in Patients of Chronic Liver Disease

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ABSTRACT

Objective: To determine the frequency of vitamin D deficiency in chronic liver disease patients.
Study design: Cross-sectional study.
Place and Duration of Study: Gastroenterology Department, Liaquat National Hospital and Medical College, Karachi Pakistan, from Jan to Dec 2020.
Methodology: Patients between the age of 18 to 50 years, of either gender, already diagnosed case of chronic liver diseases for 6 months and had sun exposure of at least 15 minutes twice weekly were included in this study. History was taken after taking informed written consent, the clinical assessment was done, and blood samples were sent for serum vitamin D levels to determine the results.
Results: The study included 177 patients with chronic liver disease. One hundred eleven patients (62.7%) were males and 66 patients (37.3%) were females, with the mean age of 45.0 ± 6.306 years. Vitamin D deficiency was observed in 100 patients (56.5%).
Conclusion: The frequency of vitamin D deficiency was quite high. It increases with age and body mass index and is predominant in the male gender, while no association was noted with sun exposure time.

Keywords: Chronic liver disease, Vitamin D levels, Vitamin D deficiency.

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INTRODUCTION

Chronic hepatitis C virus (HCV) liver disease is a general medical problem Worldwide, with 170 million people infected. An estimated international seroprevalence of about 3% is reported for 3000000 to 4000000 new HCV infections each year.[1] High percentage (46% to 92%) of these patients have low vitamin D levels, and over 25% experience severe deficiency.

Several studies have proven that low vitamin D levels considerably increase the mortality risk from all causes, along with cardiovascular diseases in the general population.[2,3] In chronic liver disease patients of different etiologies, deficiency in vitamin D is related to increased risk of death,[4,5] portal hypertension complications, bacterial infections and fibrosis severity.[6,7]

Among chronic liver disease patients, vitamin D deficiency is widespread; around 92% of patients have deficient vitamin D levels, and about 33% show extreme deficiency.[8] Even mild liver disease is affected. However, liver cirrhosis patients more commonly suffer from a severe deficiency.[9]

The study was designed to assess the frequency of vitamin D deficiency in chronic liver disease Patients. This study will give the most recent and nearby measurements of chronic liver disease promp-ted by vitamin D deficiency. Moreover, this study will help determine that patients with chronic liver diseases should have this test. This will aid early diagnosis and methodologies in chronic liver disease patients to reduce their vitamin D deficiency burden.

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METHODOLOGY

This cross-sectional study was conducted at Liaquat National Hospital Karachi's Department of Gastroenterology, from January 2020 to December 2020 after approval from the Ethical Committee (No.0490-2019-LNH-ERC) and after taking informed consent. The sample size was calculated using a population proportion sample size calculator with a prevalence of 8 (92%), confidence interval of 95%, margin of error= 4%, and the estimated sample was 177 patients.

Inclusion Criteria: Patients between the age of 18 to 50 years, of either gender, already diagnosed case of chronic liver diseases for >6 months and had sun exposure of atleast 15 minutes twice weekly were included in this study.

Exclusion Criteria: Patients with chronic liver disease taking vitamin D supplementation, patients using anti-

epileptic drugs, pregnant females, chronic kidney disease patients and patients having a history of vitamin D resistance were excluded.

Data was collected from patients meeting inclusion criteria from the Gastroenterology Department at Liaquat National Hospital, Karachi. The patient was assessed for vitamin D levels from an institutional diagnostic laboratory through blood samples following all aseptic measures by a pathologist. Levels of vitamin D in blood reports were recorded.

Statistical Package for Social Scicences (SPSS) version 20.0 was used for the data analysis. Frequencies and percentages were calculated for gender, cause of CLD (HBV/HCV/Alcohol/Wilson) and vitamin D Deficiency.

Mean and standard deviations were determined for age, SGPT, BMI, socio-economic status (monthly income), sun exposure, and vitamin D levels. Chi-square test was applied to find out the association. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

One hundred seventy-seven patients with chronic liver disease were included in this study. The mean age of the patients was 45.0 ± 6.306 years. Out of 111 patients (62.7%) were males and 66 patients (37.3%) were females (Table-I).

The mean sun exposure was 24.239 ± 5.218 mins, mean BMI was 24.239 ± 2.664 kg/m2, and mean serum SGPT level was 70.485 ± 31.429 U/L.

The cause of CLD was HBV in 25 (14.1%) patients, HCV in 142(8.3%) and alcohol in 10 patients (5.6%). The socio-economic status was <25000 PKR/month in 47 (26.6%) patients, 25000-50000 PKR/month in 116 (65.3%) and >50000 PKR/month in 14 (7.9%) patients, as presented in Table-I.

The vitamin D level was <20 ng/mL in 104 (58.8%) patients and >20 ng/ml in 73 patients (41.2%). The deficiency of Vitamin D was seen in 100 patients (56.5%).

Age groups, gender, BMI, socio-economic status, sun exposure and cause of CLD were calculated according to vitamin D deficiency.

In our study, vitamin D deficiency was strongly associated with the cause of CLD with the *p*-value of 0.034 and was not significantly associated with age (years), Gender, BMI (kg/m²), socio-economic status and sun exposure as shown in the Table-II.

Table-I: Descriptive statistics of age, sun exposure (Mins), BMI, serum SGPT levels (U/L), gender, cause of CLD, Sociso-economic status, vitamin D level, vitamin D deficiency (n=177).

Parameter	Mean ± SD / n (%)
Age	45.0 ± 6.306
Sun Exposure (mins)	24.239 ± 5.218
BMI	24.493 ± 2.664
Serum SGPT Levels (U/L)	70.485 ± 31.429
Gender	
Male	111 (62.7%)
Female	66 (37.3%)
Cause of Chronic Liver Disease	
Hepatitis B	25 (14.1%)
Hepatitis C	142 (80.3%)
Alcohol	10 (5.6%)
Total	177 (100%)
Socio-Economic Status	
<25000 rupees	47 (26.6%)
25000-50000 rupees	116 (65.5%)
>50000 rupees	14 (7.9%)
Vitamin D Level	
<20 ng/mL	104 (58.8%)
>20 ng/mL	73 (41.2%)
Vitamin D Deficiency	
Yes	100 (56.5%)
No	77 (43.5%)

Table–II: Vitamin D Deficiency to age, gender, body mass index, Socio-economic status, sun exposure & cause of chronic liver disease (n=177).

Parameters	Vitamin D Deficiency			*p*-value
	Yes, (n=100)	No (n=77)	Total	
Age				
18-33 years	5 (3%)	1 (0.6%)	6 (3.6%)	0.178
34-50 years	95 (53.5%)	76 (42.9%)	171 (96.4%)	
Gender				
Male	63 (36.5%)	48 (27.1%)	111 (62.7%)	0.928
Female	37 (20.9%)	29 (16.4%)	66 (37.3%)	
Body Mass Index (kg/m²)				
18-24	48 (28.8%)	32 (19.2%)	80 (48%)	0.604
25-30	52 (27.7%)	45 (24.3%)	97 (52%)	
Socio-Economic Status				
<25000 PKR/Month	30 (16.9%)	17 (9.6%)	47 (26.6%)	0.336
25000-50000 PKR/Month	64 (36.2%)	52 (29.4%)	116 (65.5%)	
>50000 PKR/month	6 (3.4%)	8 (4.5%)	14 (7.9%)	
Sun Exposure (Mins)				
15-26	36 (21.6%)	22 (13.2%)	58 (34.8%)	0.282
27-40	64 (34.9%)	55 (30.2%)	119 (65.2%)	
Cause of Chronic Liver Disease				
Hepatitis B	18 (10.2%)	7 (4%)	25 (14.1%)	0.034
Hepatitis C	80 (45.2%)	62 (35%)	142 (80.2%)	
Alcohol	2 (1.1%)	8 (4.5%)	10 (5.6%)	

DISCUSSION

In our study we found that frequency of vitamin D deficiency was quite high, and it increased with the increase in age and BMI and was predominant in the male gender, while no association was noted with sun exposure time. 25 (OH) Vitamin D levels should be regularly assessed in chronic liver disease patients and treated appropriately to improve the general prosperity of cirrhotic patients.

Vitamin D performs an increasingly significant function in immunity, infectious diseases, cancer, fibrosis and chronic liver diseases.[10] This hormone has been thoroughly examined in the literature for its pleiotropic effects, which include the regulation of transcription of more than 200 genes involved in cellular growth and differentiation, immunomodu-lation, inflammation and fibrogenesis, and the impact of these genes on liver disease.[10,11] Two different pools of 1,25 (OH)2D3 with distinct objectives were proposed by Han *et al*,[10] Consisting of the typical liver-kidney loop, the first pool stimulates intestinal calcium absorption by mediating the active transfer of calcium (calbindin) through the intestinal mucosa, which retains calcium homeostasis in the blood and enables the accumulation of bone calcium. The second pool contains the immune system and the local development by immune cells (monocytes, macrop-hages, dendritic cells, B and T cells and lymphocytes) of calcitriol that could lead to immune regulation (with a possible protective role against infections). Although not clearly defined, these separate pools could lead to two separate roles of homeostasis, which are endocrine and paracrine. Petta *et al,* best summarizes our present definition of vitamin D pathophysiology as" a complex interaction among liver damage, vitamin D and genetic determinants of vitamin D deficiency" in relation to liver disease/ cirrhosis.[12]

The Median vitamin D levels for CLD patients were 23.16 ng/mL (controls: 34.14 ng/mL) in our study compared to Jamil *et al*, study. In our study, 100 patients were vitamin D deficient, suggesting that many CLD patients have deficient stores of vitamin D, which could cause many musculoskeletal manifestations.[12,13] 34% of the patients found vitamin D stores deficiency (<20 ng/mL). Most chronic Liver disease patients had either inadequate or deficient levels of vitamin D, and only 12% of cirrhotic patients obtained adequate supplies of vitamin D (> 30 ng/mL). Vitamin D deficiency in cirrhotic patients has been shown in several extensive trials and studies. In a study conducted by Zhao *et al*, 345 cirrhotic patients found that their vitamin D levels were significantly deficient.[14] Further study by Fernandez *et al*, in Spain found that 87% of the 94 chronic liver disease patients had deficient 25(OH)vitamin D levels.[15] Kumar *et al*, carried out the study on 160 CLD patients and reported that 80% of patients were vitamin D deficient.[16] We observed that only 12% of patients had adequate levels of 25 (OH) vitamin D, while 88% of patients had not sufficient vitamin D levels.

There are emerging evidences suggesting the significance of vitamin D on mortality in the general population and patients with cirrhosis and hepatocellular carcinoma.[17,20] In addition, the correlation of reduced vitamin D levels with liver failure and infections promotes vitamin D used as a prognostic indicator in the cirrhotic population.[17,18] The function of vitamin D supplementation in maintaining SVR for interferon-based care patients with chronic hepatitis C is uncertain.[21,22] This should be clarified as most published studies have included healthy and normal liver function patients and mild fibrosis. The vitamin D supplements demand achievement of higher SVR levels is, however, expected to decline along with reduced use of interferon in the era of direct-acting antiviral therapy.

Current clinical guidelines address vitamin D supplementation for bone disease in liver cirrhosis and cholestatic conditions. It is of the greatest significance to explain the details regarding vitamin D supplementation, such as the threshold to start supplementation, optimal duration, method of delivery and bioavailability, dosage modification, other liver-related extra-skeletal signs, pre-treatment screening intervals, efficacy/ monitoring intervals in therapy and post-treatment surveillance intervals. The accuracy of the various 25 (OH) D measurements has to be addressed.[22,23] Vitamin D deficiency not only causes muscul-oskeletal manifestations but many more complications in cirrhotic patients as well. Vitamin D is associated with early decompensation and higher mortality rates in these patients.[24] Many studies have also shown that suitable vitamin D replacement can improve the functional condition, child-Pugh score, model of end-stage liver disease score, prognosis and overall morbidity in liver disease patients. Therefore, it is advised that this deficiency should be treated appropriately to benefit patients with chronic liver problems.[25]

CONCLUSION

The frequency of vitamin D deficiency was quite high. It increases with age and BMI and is predominant in

the male gender, while no association was noted with sun exposure time.

Conflict of Interest: None.

Author's Contribution

WA: Conception, design, Interpretation of data, MTK: Design, analysis, Interpretation of data, SK: Design, interpretation of data, HAK: Design, analysis, and interpretation of data, GM: Design, analysis, AF: Data design, Interpretation of data

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