Frequency of Vitamin D deficiency among patient with Liver cirrhosis

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ABSTRACT

Introduction: Chronic liver disease (CLD) is increasing important chronic disease worldwide It's potential impact on the patient's health, and their health-related quality of life is huge/Vitamin D deficiency is a globalpublic health concern, even in tropical regions wherethe risk of deficiency was previously assumed to below due to adequate exposure to sun. Poor vitamin D status, asindicated by low serum concentrations of 25-hydroxyvitamin D [25(OH)D] has been observed inSouth Asian populations. Initially thought to be exclusive to patients withchronic cholestatic liver disorders, it is now clear thatvitamin D deficiency and insufficiency are highly prevalentin all forms of CLD. This can be due to lowvitamin D levels due to limited sun exposure is commonamong patients with chronic illnesses and is likely animportant cause for vitamin D deficiency in cirrhosis andend stage liver disease.

Materials and Methods: This cross sectional (Descriptive Study) was performed in Medical department of Hayatabad Medical Complex, Peshawar, from 02-07-2018 to 01-01-2019. A total of 181 cases of cirrhosis were selected from OPD and serum vitamin D level was recorded.

Results: The mean age of the sample was 50.1 + 8.3 years. 65.2% were male and 34.8% were female. The mean duration of illness was 7.6 + 2.5 years. Most of the patients i.e. 45.9% were in the class B according to Child T Pugh Classification of liver cirrhosis. Mean vitamin D level of the whole sample was 17.2 + 7.4ng/dl and vitamin D deficiency (< 20ng/dl) was recorded in 56.4%.

Conclusion: Vitamin D deficiency is a common problem in our local cirrhotic population. More studies are required to develop association of vitamin D with cirrhosis after adjusting for factors which can aggravate vitamin D deficiency in cirrhotic patients.

Key Words: Liver cirrhosis, vitamin D, child T Pugh classification.

INTRODUCTION

Chronic liver disease (CLD) is increasingly being recognized as important health issue worldwide because of its epidemiological burden, its potential impact on the patient's health, and negative impact on health-related quality of life (HRQOL).1, 2CLD as a disease is taking a lot of toll on health system and economics due enormous direct and indirect cost attached to it.3, 4 Patients with chronic liver disease suffer from fatigue, loss of self-esteem, inability to function at work, anxiety, depression, and other emotional problems that profoundly decrease their quality of life and well-being.5, 6

Vitamin D deficiency is a globalpublic health concern, even in tropical regions wherethe risk of deficiency was previously assumed to below due to cutaneous vitamin D synthesis stimulatedby exposure to sun. Poor vitamin D status, asindicated by low serum concentrations of 25-hydroxyvitamin D [25(OH)D], has been observed inSouth Asian populations. 7, 8

Although initially thought to be exclusive to patients withchronic cholestatic liver disorders, it is now clear thatvitamin D deficiency and insufficiency are highly prevalentin all forms of CLD. This can be due to lowvitamin D levels due to limited sun exposure is commonamong patients with chronic illnesses and is likely animportant cause for vitamin D deficiency in cirrhosis andend stage liver disease.9 Other causes of low vitamin Dlevels in patients with CLD may includedecreased hepatic hydroxylation, increased extrahepaticuptake of vitamin D by adipose tissue, impaired intestinalabsorption, and decreased dietary intake. 10

The global prevalence of vitamin D deficiency in thegeneral population affects all age groups and rangesfrom 20 to 100%.11 The prevalence of vitaminD deficiency in patients with CLD like cirrhosis has been reported torange from 64% to 92% and is has been shown to be inversely relatedto disease progression. 12 Moreover, it has also been reported that liver transplant candidates, the frequency of vitamin D deficiency is 84%, while liver transplant resulting in a marked increase in 25(OH)D, 1 α,25(OH)2D levels.13

The present study is designed to determine the frequency of vitamin D deficiency in patients with liver cirrhosis. Local statistics are missing since no such study has been done in Peshawar and the results from literature reflects that vitamin D deficiency in cirrhotic patients varies from one settings to another. This study will provide us with

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fresh local data about the magnitude of the problem and the results of this study can be used as first hand local evidence to future research and later on recommendations can be developed for prevention and control.

MATERIALS AND METHODS

This cross sectional descriptive study was performed in department of Medicine at Hayatabad Medical Complex, Peshawar over six months from 02-07-2018 to 01-01-2019, Sample size of 181was calculated using 64%12 proportion of vitamin D deficiency in liver cirrhosis, 95% confidence interval and 7% margin of error using WHO software using non-probability consecutive sampling technique. All patients with liver cirrhosis between 18-65 years of age with minimum duration of 6 months after diagnosis were included. Patients already diagnosed of osteomalacia or vitamin D deficiency (on medical record), with Chronic renal failure (as diagnosed by specific investigations or medical records and patients on vitamin D supplementation (on medical records and history) were excluded. As the above factors are the confounders and will make the study result bias.Approval of the ethical committee was taken before starting the study. Written informed consent was obtained from all patients after explaining them the purpose and benefits of the study. From all the patients, 10cc of blood was obtained under strict aseptic technique and was immediately sent to hospital laboratory to detect vitamin D deficiency. All data was recorded in a structured proforma. Confounding factors and bias was controlled by strictly following exclusion criteria. Data was entered into SPSS version 22. Descriptive statistics was used to analyze the data. Mean ¬+ standard deviation was calculated for quantitative variables like age, serum vitamin D level and duration of illness while frequency / percentages was calculated for categorical variables like gender, grade of cirrhosis and vitamin D deficiency. Vitamin D deficiency was stratified among the age, gender, duration of illness and grade of cirrhosis to see the effect modifiers using chi square test with p value of < 0.05 as significant. All the results were presented as tables and graphs.

RESULTS

Basic demographic characteristics of study population are shown in table 1 while patient were classified according to Child classification. Table2. The mean vitamin D level of the whole sample was 17.2 + 7.4ng/dl. According to operational definitions, the vitamin D deficiency (vitamin D level < 20ng/dl) was recorded in 56.4% of patients while we stratified vitamin D levels with regards to age, gender, duration of illness and severity of cirrhosis (Table 3,4).

Table 1: Basic Demographic Characteristics of study population (n=181)

	n	Range	Min	Max	Mean	Std. Dev
Age	181	30.00	35.00	65.00	50.1	8.3

		Frequency	Percent
Age Groups	35 to 45 years	56	30.9
	> 45 to 55 years	88	48.6
	> 55 to 65 years	37	20.4

Gender	Male	118	65.2
	Female	63	34.8

Duration of illness	3 to 6 years	65	35.9
	> 6 to 9 years	60	33.1
	> 9 to 12 years	56	30.9

Table 2: SEVERITY OF CIRRHOSIS AS PER CHILD T PUGH CLASSIFICATION (n=181)

Severity of cirrhosis		Frequency	Percent
	Class A	52	28.7
	Class B	83	45.9
	Class C	46	25.4
	Total	181	100.0

Table 3: Vitamin D Deficiency, Gender and Age Satisfaction (n=181)

		Frequency	Percent
Vitamin D Deficiency	Yes	102	56.4
	No	79	43.6
	Total	181	100.0

		Vitamin D Deficiency		p value
		Yes	No	
Age Group	35 to 45 years	30	26	0.009
		53.6%	46.4%	
	> 45 to 55 years	43	45	
		48.9%	51.1%	
	> 55 to 65 years	29	8	
		78.4%	21.6%	
Total		102	79	
		56.4%	43.6%	

Gender of the Child	Male	82	36	< 0.001
		69.5%	30.5%	
	Female	20	43	
		31.7%	68.3%	
Total		102	79	
		56.4%	43.6%	

Duration of Cirrhosis	3 to 6 years	49	16	< 0.001
		75.4%	24.6%	
	> 6 to 9 years	24	36	
		40.0%	60.0%	
	> 9 to 12 years	29	27	
		51.8%	48.2%	
Total		102	79	
		56.4%	43.6%	

Table 4: SEVERITY OF CIRRHOSIS WISE STRATIFICATION OF VITAMIN D DEFICIENCY

		Vitamin D Deficiency		p value
		Yes	No	
Severity of cirrhosis (Child T Pugh)	Class A	45	7	< 0.001
		86.5%	13.5%	
	Class B	29	54	
		34.9%	65.1%	
	Class C	28	18	
		60.9%	39.1%	
Total		102	79	
		56.4%	43.6%	

DISCUSSION

The high prevalence of vitamin D deficiency in this population occurs regardless of the etiology of liver disease.14,15Synthetic liver dysfunction is not entirely responsible, as vitamin D deficiency is still highly prevalent in those with non-cirrhotic liver disease.16 25(OH)D levels normalize after oral or parenteral administration of vitamin D in patients with cirrhosis, indicating that 25-hydroxylation is preserved in this patient population. 17,18 Serum DBP levels, which play a critical role in the transport and bioavailability of vitamin D, are moderately decreased in cirrhosis. 19,20 However, as only 5% of DBP binding sites are occupied at any one time with vitamin D metabolites1,21 profound liver dysfunction is required for low DBP levels to exert a significant contributing role to vitamin D deficiency in chronic liver disease. Vitamin D deficiency in CLD is likely to result from a number of mechanisms. Patients with a chronic medical illness such as CLD are more likely to have lower levels of sunlight exposure and/or inadequate dietary intake of

vitamin D. Moreover, luminal absorption of dietary sources of vitamin D may be hindered by intestinal edema complicating portal hypertension and/or impaired bile salt dependent micellar incorporation due to cholestasis.

The global prevalence of vitamin D deficiency in the general population affects all age groups and ranges from 20 to 100% when referring to serum 25(OH)D concentrations < 20 ng/ml.22 The prevalence of vitamin D levels < 20 ng/ml in CLD has been reported to range from 64 to 92% and is commonly inversely related to disease progression. 23 Some studies, however, have failed to find a difference in vitamin D status between patients with cirrhosis and those without, 24 illustrating that the cause of this deficiency must be multifactorial. Previously, vitamin D deficiency was thought to be predominantly found in cholestatic liver disorders because of impaired intestinal absorption commonly observed in such patients. 25 Accumulating evidence, however, supports its widespread presence in CLD, regardless of etiology. For a detailed review of vitamin D specifically regarding the hepatitis C virus (HCV), please refer to Cholongitas et al.26, Arteh et al27. found vitamin D < 32 ng/ml (i.e. 80 nmol/L) in 92% of 118 patients with CLD (HCV cirrhosis, n = 43; HCV without cirrhosis, n = 57; non-HCV-related cirrhosis, n = 18). Likewise, Fisher et al. found inadequate 25(OH)D levels (< 32 ng/ml) in 91% of patients with non-cholestatic CLD, and the majority (68%) were vitamin D-deficient (< 20 ng/ml). Patients in Child-Pugh class C had significantly (P < 0.001) lower mean 25(OH)D concentrations than patients in class A. These findings are supported by Chen et al,23Miroliaee et al 28 and Rode et al, 29 who found 75% of patients with cirrhosis to have 25(OH)D levels < 20 ng/ml. Most recently, Putz-Bankuti et al, 30 reported an inverse association (r = _0.21, P = 0.08) between serum 25(OH)D levels and the severity of liver disease in a cohort of 75 patients with cirrhosis. Interestingly, the authors also investigated survival in this cohort and 32% of patients had died during a median follow-up period of 3.6 years. Kaplan–Meier curves demonstrated a significantly (P < 0.001) increased mortality with low vitamin D concentrations. The publish data reflect that subjects in Child-Pugh class C have approximately half the 25(OH)D concentrations of class A, 30,31 and in most cases, the difference is statistically significant (P < 0.01). A low vitamin D status is also evident in patients with other chronic liver diseases, particularly in the presence of cirrhosis. For instance, 50 patients with non-alcoholic steatohepatitis (NASH) and 10 patients with simple steatosis were observed by Targher et al.32 to have lower 25(OH)D concentrations compared with 60 controls matched for age, gender and body mass index (BMI). Overall, this Italian-based study found lower vitamin D status in patients with non-alcoholic fatty liver disease (NAFLD), which was also associated with histopathological NAFLD features. These findings were recently corroborated by the same group 33 in a larger study (n = 262), in which low 25(OH)D levels were independently associated with NAFLD (n = 162) and were significantly (P < 0.001) lower than in subjects who were free from NAFLD and other liver diseases (15 ± 9 vs. 21 ± 9 ng/ml). Of note, when compared with the highest quartile, subjects in the lowest quartile of serum 25(OH)D levels displayed an odds ratio (OR) of 4.7 (95% confidence interval (CI), 2.2–10.3, P < 0.001) for NAFLD.

As would be expected, liver transplant patients exert a different pattern: Trautwein et al 34 found that 96% of these patients had inadequate vitamin D stores pretransplant but that post-transplant, vitamin D deficiency was uncommon. Having normal vitamin D levels pretransplant may, however, have important implications for this patient group. A study by Bitetto et al 35 found pretransplant low serum 25(OH)D levels (< 12.5 ng/ml) to predispose to rejection episodes; the authors believe that supplementation with vitamin D might prevent acute cellular rejection via improved immune tolerance.

Current guidelines have not specifically addressed if vitamin D levels should be checked in patients with liver disease attending ambulatory hepatology clinics. However, it is important to measure serum 25 (OH) vitamin D levels in patients with chronic liver disease and cirrhosis periodically. If serum levels of 25(OH) vitamin D are <20 ng/mL, it is important to administer 5,000 IU of vitamin D3 daily or 50,000 IU of vitamin D2 or D3 weekly for 3 months, followed by 1,000 IU/day indefinitely.

CONCLUSION

Vitamin D deficiency is a common problem in our local cirrhotic population. More studies are required to develop association of vitamin D with cirrhosis after adjusting for factors which can aggravate vitamin D deficiency in cirrhotic patients.

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