Original Research Article

Vitamin D Levels in Chronic Liver Disease-A Clinical Study

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Abstract

Background: According to numerous researches conducted earlier, Vitamin D deficiency with low dietary calcium intake in the Indian population. In addition to low dietary intake, Vitamin D deficiency is also present in people diagnosed with liver, kidney, skin and ortho disorders. Because of many factors, Vitamin D deficiency is a universal concern. **Aims:** We aim to assess and compare vitamin D disease trends in a group of patients with non-cholestatic CLD. **Materials and methods:** It is hospital-based cross sectional study was performed in Government General Hospital Suryapet, Telangana, from 2018 to 2019, the research period was one year. Cases with Non-cholestatic Chronic Vitamin D deficiency Class with hepatic disease with age & gender. In each category, we increased the sample size to 80 patients. **Results:** Prevalence of vitamin D deficiency and insufficiency were 36% and 48.8% respectively among CLD patients. In present study, we selected 80 patients in which 65 (81.3%) were males and 15 (18.7%) were females, with mean age 45±12.1 years. 60 (75%) of the cases were diagnosed with alcoholic CLD (60 males). Vitamin D deficiency <10 ng/dl is observed in 4 cases(5%), 10-20 ng/mL in 25 cases(31.2%), 21-30 ng /mL is seen in 39 cases (484.%) and >30 ng/mL in 12 cases(15%). Low vitamin D levels were significantly associated with a higher MELD value($p<0.05$). The mean vitamin D level was 31+4.1 with Child-Pugh Class A (n=9), 23+5.1 with Class B (n=48) and 15.1+6.9 with Class C (n=33). With increased severity of cirrhosis, there was a strong trend towards lower vitamin D levels ($p<0.05$).**Conclusion**: In conclusion, considering the high prevalence of deficiency of vitamin D in chronic liver disease patients, it seems appropriate to conduct periodic screening to assess the extent of vitamin D in this population.

Keywords: Chronic liver disease, Vitamin D deficiency, Non-Cholestatic CLD.

Introduction

Vitamin D is essential steroid like hormone with proven effect on homeostasis of calcium, but currently there is growing awareness deficiency of Vitamin D which has immunomodulatory and anti-inflammatory effects and is also involved in cell proliferation and differentiation. In several causes of chronic liver disease, vitamin D deficiency has been documented commonly and has been linked with the development and evolution of non-alcoholic fatty liver disease (NAFLD) and chronic hepatitis C (CHC) virus infection. The role of vitamin D in the pathogenesis of CLDs is not fully understood, but the involvement of vitamin D in the activation and regulation of both the innate and adaptive immune systems, as well as its antiproliferative effect, appears to explain the importance of vitamin D in these liver diseases. According to numerous studies published earlier, it has been reported that 1 billion people worldwide have vitamin D deficiency or insufficiency. [1] According to numerous studies published earlier, there is a widespread prevalence to differing degrees (50-90 percent) to vitamin D deficiency with poor dietary calcium intake in the Indian population.[2] In addition to low dietary intake, individuals suffering from liver, kidney, skin diseases, alcoholics and inflammation. It is interesting that processes such as the regulation of metalloproteinase synthesis and its inhibitors, the activation of fibroblasts and the synthesis of collagen are also known to be vitamin D properties. This data indicates that vitamin D may play a role in the progression of liver damage and CLD. In this review, we intended to assess and compare vitamin D disease trends in a group of patients with non-cholestatic CLD, given that there are limited studies on vitamin D status in patients with non-cholestatic CLD.

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Materials and Methods

In the Biochemistry Department, hospital-based cross sectional study was performed. From September 2018 to December 2019, the research period was one year. Cases with Non-cholestatic Chronic Vitamin D Deficiency Class with liver disease with age and gender. In each category, we increased the sample size to 80 patients. Samples of venous blood were collected after an overnight 10-around 12 hr of fasting.

Inclusion criteria: Both genders of diagnosed non-cholestatic non-cholestatic chronic liver diseases; patients with concomitant HCV, HBV, HIV, hepatic or extra hepatic malignancies, inflammatory bowel disorders, celiac disease, and history of total parenteral nutrition during the previous 3 months.

Exclusion criteria: Patient on medications for Supplements like vitamin D or calcium, bisphosphonates, Calcitonin, corticosteroids or hormone replacement therapy, Anti-viral medicine.

Sample size calculated by

Precision= 10.00%

Prevalence = 40.00 %

Population size= infinite

95% Confidence Interval specified limits [30% -- 50%] (These limits equal prevalence plus or minus precision)

Estimated sample size: n = 93

According to Bal Kishan Gupta et al[3] study 40 % is prevalence. Clearance from Ethics was taken before starting the study. As per proforma, all patients were investigated to clinical and laboratory examination. Both patients underwent full blood counts, blood sugar, liver function test, renal function test, PT-INR, HBsAg, ANTI-HCV, abdominal USG, and upper GI endoscopy. CLD severity was specified in accordance with Child Pugh criteria and MELD system[4,5]. The MELD system offers a more objective way to measure the severity of the disease and has less centres differences than the Child-Pugh score and a broader range of values.Checked for liver function: complete and clear bilirubin, ALT, AST, GGT, albumin, phosphatase alkaline (ALP), PT, PTT and INR. Electrolytes, phosphate and Serum calcium levels were corrected for the concentration of albumin.Vitamin D; 25(OH) level was tested using batched electro chemiluminescence immunoassay 25(OH) D total assay, and readings were categorized as:

- Normal (>30 ng/ml).
- Insufficient (20-30 ng/ml)
- Deficient (<20 ng/mL)

The data collected was coded, analysed, processed and tabulated by the Social Sciences Statistical Package (SPSS) version 20. Frequency distribution, percentage and descriptive statistics were measured, including mean±SD.

Results

In our study, we included 80 patients in which, 65 (81.3%) were males and 15 (18.7%) were females, with mean age 45±12.1 years**.**

Table 1: Demographic Distribution of levels of vitamin D

Parameters	**Vitamin D levels**			
	<10	10-20	21-30	>30
Number of patients(n=100)(%)	4(5%)	25(31.2%)	39(48.8%)	12(15%)
Gender				
Males, n(%)	4(5%)	19(23.7%)	34(42.5%)	8(10%)
Females , n(%)		6(7.5%)	5(6.2%)	4(5%)
Mean age	45+9	48.9+11	43+10	42+8
Age(in years)				
18-30	1(1.2%)	3(3.7%)	7(8.75%)	3(3.7%)
31-50	2(2.5%)	12(15%)	13(16.2%)	7(8.7%)
>51	1(1.2%)	10(12.5%)	19(23.7%)	2(2.5%)
Total	4(4.9%)	25(31.2%)	39(48%)	12(14..6%)

Prevalence of vitamin D deficiency and insufficiency were 36% and 48.8% respectively among CLD patients. Sixty (75%) of the cases had alcoholic CLD (60 males) and 8 males were 18-30 years of age, 32 were 31-50 years of age, and 20 were > 55 years of age. This suggests that lower vitamin D levels have been associated with increased age ($p<0.05$).

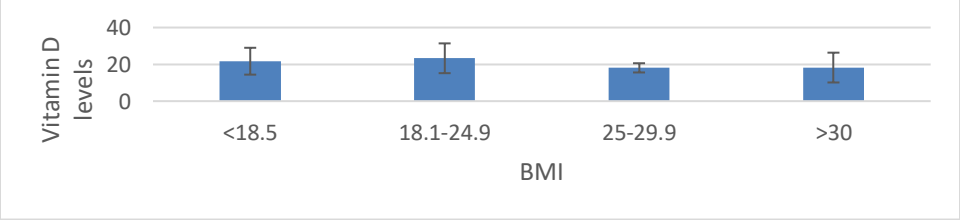

Fig 1: Relationship of vitamin-D with BMI

The mean vitamin D was 21.7 ± 7.3 for BMI patients < 18.5 (n=5), 23.3 ± 8.1 for BMI patients 18.5-24.99 (n=68), 18.1 ± 2.5 for BMI patients 25-29.99 (n=6) and 17.7 ± 9 for BMI patients > 30 (n=1) ($p>0.05$). In obese patients, we observed an inverse association between the mean vitamin D level and BMI, with the lowest mean vitamin D level.Mean levels of vitamin D were 26.1 ± 6.9 at bilirubin < 2 mg / dl (n=30), 22.1 ± 3.91 at bilirubin 2-3 mg / dl (n=12) and 19.24 ± 6.91 at bilirubin > 3 mg / dl (n=38). The mean amount of vitamin D decreases when the amount of bilirubin increases ($p<0.05$).

Table 2: Comparison of relation to MELD score with vitamin D level

Parameter	**MELD score**	

	<9(n=2)	10-19(n=39)	20-29(n=24)	30-39(n=13)	>40(n=2)	P-value
Vitamin-D Mean±SD	33.4+2.3	25.3+6.1	20+7.1	15.1+3.9	8.2+0.9	<0.00

The mean amount of vitamin D was 33.4 ± 2.3 with MELD < 9 (n=2), 25.3 ± 6.1 with MELD 10-19 (n=39), 20 ± 7.1 with MELD 20-29 (n=24), 15.10 ± 3.9 with MELD 30-39 (n=13) and 8.2 ± 0.9 with MELD > 40 (n=2). Low vitamin D levels were significantly correlated with a higher MELD ($p<0.05$) level.

Table 3: Comparison of the mean value of the level of vitamin D with the Child-Pugh Score

Parameter	Child-Pugh Score			
	Class A (5-6) (n=9)	Class B(7-9) (n=48)	Class C(10-15)(n=33)	P-value
Vitamin-D Mean± SD	31+4.1	23+5.1	15.1+6.9	<0.00

With Child-Pugh Class A (n=9), the mean vitamin D level was 31 + 4.1, 23 + 5.1 with Child-Pugh Class B (n=48) and 15.1 + 6.9 with Child-Pugh Class C (n=33).With the growing incidence of cirrhosis, there was a strong trend towards lower vitamin D levels ($p<0.05$).

Discussion

In our sample, 80 patients with prevalence of vitamin D deficiency and insufficiency were 36% and 48.8% respectively among CLD patients and mean age of 45±12.1 years were enrolled. Sixty-five (81.3%) were men and the remaining 15 (18.7%) were women. In our study, 60 (75%) of the cases were alcoholic CLD (60 males) and in this study, 8 males belonged to the 18-30 age group, 32 to 31-50 years, and 20 were > 55 years of age.In females, we found a low prevalence of CLD, which correlates with Bal Kishan Gupta.[3] Out of them, 91 (91%) were males, and the remaining 9 (9%) were females. The mean age was 47±11 (males) and 44+18 (females) respectively. The group of subjects with alcohol-related CLD was the group with the more vitamin D deficiency, with mean levels of 14ng /mL, similar to the findings previously described in our cohort by Malham et al.[6] This is possibly attributed to the higher number of alcoholic cirrhotic patients in our environment and the established correlation between alcoholic cirrhosis and malnutrition, which could be a coadjuvant cause for Vitamin D deficiency.[7] Previous studies have also shown that decreased levels of vitamin D are closely linked to the level of malnutrition in patients with CLD. 2677 (77 percent) of the cases suffered from alcoholic CLD (76 males and 1 female). In comparison to the previous research conducted by Putz Bankuti C et al. [8], our analysis is because alcoholic CLD belongs to most of the cases in our sample and alcoholism is common in males but very rare in our region in females. Our study out of 80 patients Vitamin D deficiency <10 ng/dLis observed in 4 cases(5%), 10-20 ng/mL in 25 cases(31.2%), 21-30 ng/mL is seen in 39 cases (484.%) and >30 ng/mL in 12 cases(15%) which is in agreement with Bal Kishan Gupta. et al[3] study Vitamin D deficiency (10-30 ng / dl)observed in 43 (43%) patients, of which 5(5%) suffered from extreme vitamin D deficiency (< 10 ng / dl). Vitamin D insufficiency (21-29.9 ng/dl) was observed in 42(42%). Thus, in 85 (85 percent) patients, vitamin D levels were below average. Similar findings were made by previous studies.[9-11] Potential reasons for vitamin D deficiency in CLD may be attributed to reduced vitamin D hydroxylation and development of vitamin D binding protein (DBP), inadequate sun exposure, inadequate food consumption, steroid use, jaundice-related degradation of vitamin D synthesis in the skin and decreased absorption of vitamin D caused by the intestine.With the Child-Pugh score and MELD score, we observed a strong negative correlation. The increased incidence of liver disease was associated with such low levels of 25(OH)D. Bal Kishan Gupta et al[3]has provided similar observations. We also found that low levels of vitamin D were associated with poor results similar to those of Finkelmeier F et al.[11] Thus, our findings suggest that vitamin D in CLD can be both a biomarker of severity and a potential therapeutic target.It is important to treat all CLD patients that are Vitamin-D deficient. It should be remembered, however, that Vitamin-D therapy is not without its dangers, as excessive consumption can induce mild toxic effects, as nausea, fatigue, constipation and irritability, and even extreme consequences, such as symptomatic hypercalcaemia, bone loss or renal calculi. In a review of 108 HCV patients, Ladero et al.[12] found that average Vitamin-D levels were all reached after vitamin supplementation. We did not provide care to patients in our sample, but the therapy also seems to be effective, because while the target dose (100ng / mL) was surpassed in some cases, no signs of toxicity were recorded. It should be remembered that laboratory studies after discontinuation of therapy in patients in which a Vitamin-D level of 100ng / mL was exceeded revealed that the Vitamin-D returned to ideal levels of about 50ng /mL.

Conclusion

High prevalence of vitamin D deficiency and insufficiency among CLD patients. Our research concludes that CLD is correlated with a substantially decrease vitamin D level that is independent of gender and BMI. Deficient vitamin D levels are associated with CLD incidence of infection. The results of our study indicate that understanding of the amount of serum vitamin D in CLD patients is significant. In order to confirm the value of vitamin D levels in CLD patients, further studies are needed by contrasting normal healthy subjects with controls and by interfering in the type of vitamin D supplementation in CLD subjects. In conclusion, given the high prevalence of vitamin D deficiency in patients with CLD, it seems appropriate to conduct periodic screening to assess the extent of vitamin D in this population.

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