Vitamin D Levels and Severity of Cirrohosis: A Cross Sectional Study

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Original Research Article

ABSTRACT

Low 25(OH) vitamin D concentration is observed to be associated with liver dysfunction and predict hepatic decompensation and mortality in patients with chronic liver disease. The objectives of the study were to estimate serum vitamin D levels in patients with chronic liver disease; to find out the severity of cirrhosis according to Child Pugh Classification and to find out the relationship between severity of cirrhosis (Child Pugh) with levels of serum Vitamin D. This cross sectional study was conducted amongst 100 patients presenting with cirrhosis of liver to OPD or admitted in a tertiary care hospital during study period year 2017-2018. Details regarding socio-demographic variables and history were obtained followed by physical and biochemical examination. Data was compiled using MS excel and analysed using Epi Info 7.2 software. Majority of the patients were in the age group 41-60 years with male preponderance. Mean Vitamin D level estimated in the study being 13.9±7.7 was highest in the Child Pugh Class A and lowest in the Child Pugh Class C. The association of mean Vitamin D in relation to Child Pugh Class was found to be statistically significant ($p<0.05$). The present study found low levels of Vitamin D in patients with cirrhosis. The severity of cirrhosis as assessed by Child Pugh Score was inversely proportional to the Vitamin D level.

KEY WORDS: Cirrhosis, Child Pugh score, Vitamin D,

Abbreviations: 25(OH)D: 25-hydroxyvitamin D , UV-B: ultraviolet B, NAFLD: Non-Alcoholic liver disease, OPD: out patient department.

INTRODUCTION:

Vitamin D is important for calcium homeostasis and ensures adequate calcium supply for bone mineralisation by its effects on bone, kidney, and gut.[1] The liver plays crucial role in vitamin D metabolism because hepatic 25-hydroxylation, catalyzed by cytochrome P450 2R1 (CYP2R1), is required to convert vitamin D to 25-hydroxyvitamin D (25(OH)D).[2] 25(OH)D is the main circulating vitamin D metabolite used to classify vitamin D status. It best reflects vitamin D supply by nutrition, supplements, and UV-B-induced vitamin D synthesis in the skin.[3] Most patients with chronic liver disease and cirrhosis have insufficient serum levels of 25 (0H) vitamin D.[4] Initially it was thought that patients with cholestatic liver disease are more likely to be vitamin D deficient, but it is observed that patients with parenchymal liver diseases such as alcoholic liver disease, NAFLD, and chronic hepatitis C are also at risk for low vitamin D levels.[5]

Low 25(OH) vitamin D concentrations are found to be associated with liver dysfunction and predict hepatic decompensation and mortality in patients with chronic liver disease.[6] Various studies suggest that vitamin D effects may play a significant role in the pathogenesis of chronic liver diseases. It has been studied that vitamin D exerts anti-inflammatory and anti-infectious effects and may protect against autoimmunity e.g. by upregulation of regulatory T cells. Interestingly, poor vitamin D status is linked to severe fibrosis and low responsiveness to interferon therapy in patients with chronic hepatitis C.[7,8]

Interventional studies on vitamin D supplementation in patients with liver diseases are scarce and have shown mixed results on the effects of vitamin D on parameters of mineral metabolism, liver function, and fibrosis. However, it is important to evaluate vitamin D effects in the setting of cirrhosis in order to guide clinical decisions and provide a basis for the development of vitamin D recommendations in these patients. The objectives of this study include the estimation of serum vitamin D levels in patients with chronic liver disease, assessment of severity of cirrhosis according to Child Pugh Classification and

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Table 1: Distribution of patients according to socio-demographic variables.

Socio-demographic variables		Frequency	Percentage
Age Group (years)	15-20	4	4
	21-40	30	30
	41-60	52	52
	61-80	10	10
	>80	4	4
Gender	Female	28	28
	Male	72	72
Occupational status	Light worker	46	46
	Moderate worker	34	34
	Heavy worker	20	20
Total		100	100

understanding the relationship between severity of cirrhosis with levels of serum Vitamin D.

MATERIAL AND METHODS:

This cross sectional study on cirrhotic patients presenting to OPD or getting admitted in the Department of Medicine, People's College of Medical Sciences and associated People's Hospital, Bhopal for a period of 6 months from December 2017 to May 2018.

One hundred patients were selected using convenient sampling. The inclusion criteria was age >18 years and known/ established cases of cirrhosis by ultrasound abdomen. Patients with the history of chronic alcoholic liver disease, osteoporosis, chronic kidney disease, diabetic patients, patient not willing for study and patients taking vitamin D supplements were excluded from the study.

After obtaining ethical clearance from the Institutional Ethics Committee, the informed consent was obtained from the study participant. Details regarding socio-demographic variables and relevant history was elicited, with particular attention to alcohol intake or osteoporosis or intake of supplements, to assess the various risk factors for liver cirrhosis. Data was recorded in pretested semi structured questionnaire. Each patient was examined physically to assess the general condition and the vital data was recorded. Per abdominal examination was done according to the standard protocol and the findings were documented. Based on the severity of the signs and symptoms and the USG reports, the treatment modality was decided. Biochemical analysis including Vitamin D level estimation and histopathology was also done.

Data was compiled using MS excel and analysed using Epi Info 7.2 software. Appropriate statistical tests were applied.

Table 2: Distribution of patients according to ascites.

Ascites	Frequency	Percentage
Absent	19	19
Mild	37	37
Minimal	1	1
Moderate	15	15
Moderate to gross	3	3
Gross	25	25
Total	100	100

RESULTS:

Majority of the patients belonged to the age group 41-60 years (52%) followed by 21-40 years (30%). Male preponderance was observed in the study. Majority of the patients were having mild ascites (37%), followed by gross ascites (25%). Whereas no ascites was observed in 19% patients. Majority of the patients were in the Child Pugh Class B (49%), followed by Class C (32%) whereas only 19% patients belonged to Child Pugh class A. Mean Vitamin D level in present study was estimated to be 13.9±7.7.

In Class A, the mean vitamin D level was 23.65 ± 9.44 mcg, in Class B it was 14.37 ± 5.66 mcg and in Class C it was 8.27 ± 3.96 mcg. The mean Vitamin D was highest in the Child Pugh Class A and lowest in the Child Pugh Class C. The comparison of mean Vitamin D in relation to Child Pugh Class was found to be statistically significant ($p<0.05$).

To find out the pairwise comparison, post hoc Tukey test was applied. The pairwise comparisons were done between the pairs – Class A – Class B; Class A – Class C and Class B – Class C. The mean Vitamin D level was higher in the Child Pugh Class A in comparison to

the Child Pugh Class B ($p<0.05$). The mean Vitamin D level was higher in the Child Pugh Class A in comparison to the Child Pugh Class C ($p<0.05$). The mean Vitamin D level was higher in the Child Pugh Class B in comparison to the Child Pugh Class C ($p<0.05$).

Table 3: Distribution of patients according to Child Pugh Class.

Child Pugh Class	Frequency	Percentage
Class A	19	19
Class B	49	49
Class C	32	32
Total	100	100

Table 4: Comparison of mean Vitamin D in relation to Child Pugh Class.

Child Pugh Class	Frequency	Vitamin D Mean	SD	f value	p value
Class A	19	23.65	9.44		
Class B	49	14.37	5.66	18.021	0.001 *
Class C	32	8.27	3.96		
Total	100				

One-way ANOVA applied. P value = 0.001, Significant

Table 5: Post-hoc Tukey.

Pair	p value	Interpretation
Class A – Class B	0.001	Significant
Class A – Class C	0.001	Significant
Class B – Class C	0.006	Significant

DISCUSSION:

Vitamin D deficiency is associated with advanced stages of hepatocellular carcinoma and poor prognosis. Majority of patients (52%) were in age group 41- 60 years followed by 21- 40 years (30%). Male patients were higher (72%) than females (28%). The mean age of patients in a study by Rech MA et al (2017) was 58.8 ±9.2 years and 53.3% patients were males.[9]

Child-Pugh score (CPS) is an independent prognostic marker for complications of pulmonary arterial hypertension and also in predicting mortality in patients with cirrhosis.[10] The Child-Pugh score is still considered the prognostic marker of cirrhotic patients.[11] In present study, majority of patients were in Child Pugh Class B (49%) followed by Child Pugh Class C (32%). In a study by Haq MI et al (2016), 17 (17%) patients were in Child Pugh class A and 35 (35%) were in Child Pugh class B and 48 (48%) were in Child Pugh class C.[12]

Mean vitamin D level in present study amongst patients with Child Pugh Class A was 23.65 ± 9.44 mcg, in Class B it was 14.37 ± 5.66 mcg and in Class C it was 8.27 ± 3.96 mcg. The mean Vitamin D was highest in the Child Pugh Class A and lowest in the Child Pugh Class C. The association of mean Vitamin D with Child Pugh Class was found to be statistically significant ($p < 0.05$) in present study. Jamil Z et al (2018) in their case control study also observed similar findings. Vitamin D deficiency was also common in the cirrhotic patients. Vitamin D deficiency was found in 34.4% patients with cirrhosis as compared to controls. The reference study also found that vitamin D levels were negatively correlated with both model of end-stage liver disease score and CP score, suggesting that as the disease advances vitamin D levels become more deficient ($p <0.05$).[13] Fernandez et al.[14] (2015) and Zhao et al[15] (2016) also found that vitamin D decreases further as cirrhosis of liver advances. Thus, patients with higher scores in the CP classification and model of end-stage liver disease score have notably lower vitamin D levels compared to patients with lower CP and model of end-stage liver disease scores.

In present study, the association between Vitamin D level was also observed between Child Pugh classes using post hoc Tukey test. The mean Vitamin D level was higher in the Child Pugh Class A in comparison to the Child Pugh Class B ($p<0.05$) and Class C ($p<0.05$). Also the mean Vitamin D level was higher in the Child Pugh Class B in comparison to the Child Pugh Class C ($p<0.05$). Though the cause of vitamin D deficiency in cirrhotic patients is multifactorial, the main mechanism through which cirrhosis of the liver causes vitamin D deficiency is the inhibition of vitamin D hydroxylation.[13]

CONCLUSION:

The present study found low levels of Vitamin D in patients with cirrhosis. It also observed that the severity of cirrhosis as assessed by Child Pugh Score was inversely proportional with Vitamin D level.

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