Original Article

Correlation of Serum Vitamin D3 level with Severity of Liver Dysfunction in Cirrhotic Patients

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Abstract:

Background: Vitamin D3 is a steroid hormone, which is mostly known as a regulator of calcium and bone metabolism. It has a significant role in the natural history of chronic liver diseases, such as chronic hepatitis C and non-alcoholic fatty liver disease (NAFLD). The deranged metabolism of vitamin D3 in liver cirrhosis was mainly attributed to impaired 25(OH)-vitamin D3 hydroxylation of the precursor vitamin D3 due to insufficient liver function. This study focused on the association of hepatic insufficiency with bone demineralization, osteomalacia, osteoporosis and minerals metabolism. **Objective:** To find out the correlation of serum Vitamin D3 level with severity of liver dysfunction in cirrhotic patients. **Methods:** A six-month Cross sectional study carried out at the department of Hepatology and Medicine, Comilla Medical College. Ethical approval from the institutional review board was obtained to ensure patient privacy and confidentiality. **Results:** Among 50 patients where male was 38 (76%) and female was 12(24%) male to female ratio was 3.16:1. Age group distribution revealed most patients were affected at middle age groups 31-40 years 12(24%) and 41-50 years 15(30%). From the age distribution of the patients, it was found that highest number of patients was in the age group of 41-50 years. Correlation of Child Pugh grading with vitamin D3 level revealed in CP A had mean vitamin D3 was 27.50, in CP B had 27.36 and in CP C had 21.42. The results showed that a significant relationship was observed between Child Pugh classification and different vitamin D3 levels; on that basis, there was a trend of lower vitamin D3 level with cirrhosis increase severity. **Conclusion:** In conclusion there is a strong trend towards vitamin-D3 levels predicting severity in patients with cirrhosis and a low value seems to identify patients at higher risk for more severity. Correlation of vitamin D3 level and CLD severity is found statistically significant, the clinical implication of vitamin D3 therapy in chronic liver disease may make a therapeutic benefit to the patient.

Keywords: Vitamin D3,Liver dysfunction, Chronic liver disease, Child-Pugh score, MELD score, Cirrhosis.

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Introduction:

Vitamin D3 is a steroid hormone, which is mostly known as a regulator of calcium and bone metabolism. However, Vitamin D3 has pleiotropic effects including cellular proliferation, differentiation and immunomodulation[1]. These extra-skeletal effects have been related to the pathogenesis and treatment of infections, cardiovascular, autoimmune and degenerative diseases and several types of cancer[2]. It has also significant role in the natural history of chronic liver diseases, such as chronic hepatitis C and non-alcoholic fatty liver disease (NAFLD)[3]. Vitamin D2 and Vitamin D3, absorbed in the intestine by biliary acids and then transported via chylomicrons to the circulation[4-6]. Vitamin D3 that comes from dietary sources or skin synthesis can be stored in the adipocytes

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or it may undergo hepatic 25-hydroxylation[5]. Vitamin D3is bound to vitamin D-binding protein (DBP) or albumin and it is transferred to the liver, where 25-hydroxylation takes place. Eighty eight per cent of 25(OH)D is bound to DBP, a protein synthesized by the liver and a member of the albumin gene family, homologous to albumin and α-fetoprotein[5]. VDR regulates the expression of more than 200 genes and, thus, influences cell proliferation, differentiation, apoptosis, immunomodulation and angiogenesis[7]. Vitamin D3 has an important role in various chronic diseases, such as infectious and cardiovascular diseases, diabetes mellitus and some types of cancer[8]. In addition, vitamin D3 has been associated with chronic liver diseases and it has been reported that low vitamin D3 status is a common feature in different types of liver diseases[9,10].

According to recent studies, the prevalence of vitamin D3 insufficiency and deficiency is higher in patients with chronic liver disease than in general population ranging between 64 and 92% 1[1,12]. It has been also reported that the incidence of vitamin D3 deficiency increases as the liver disease progresses[11,12]. According to BarchettaET AL[13] patients with NAFLD had lower 25(OH)D than controls (14.8±9.2 versus 20.5±9.7 ng/mL). The deranged metabolism of vitamin D3 in liver cirrhosis was first reported in the late '70s[14] and it was mainly attributed to impaired 25(OH)-vitamin D3 hydroxylation of the precursor vitamin D3 due to insufficient liver function[14]. Before the year 2000, the majority of the studies on vitamin D3 in cirrhosis[15] focused on the association of hepatic insufficiency with bone demineralization, osteomalacia, osteoporosis, minerals metabolism/equilibrium (calcium, phosphorus), possible endocrine disturbances (parathormone-secondary hyperparathyroidism) and, in general, with the homeostasis involving the liver- kidney-gut-calcium axis. In the past two decades, there have been considerable advances in the understanding of the pathophysiology of vitamin D3 and its possible clinical implications in chronic liver diseases[16].

A number of studies have supported the prevalence of hypovitaminosis D3 in chronic liver disease and cirrhosis[17] with one study[18] reporting a low prevalence of 25(OH)D deficiency in a cohort of patients with genotype 1 chronic HCV infection and compensated liver disease (15% cirrhotic patients): 48% and 16% of the cohort had vitamin levels of <75 nmol/L and <50 nmol/L respectively. The aim of this study is to correlate serum vitamin D3 level with the severity of liver dysfunction.

Methods: A Cross sectional observational study from January'2020 to July'2020 in the department of Hepatology and Medicine Cumilla Medical College Hospital, Cumilla. Patients diagnosed as cirrhosis attending the OPD or admitting in the Department of Medicine and Hepatology and Gastroenterology of Cumilla Medical College Hospital.Proportion of patients with cirrhosis is unknown in our setting. 50 cases of CLD patients of cirrhosis (Clinical, biochemical and sonologic evidence) was taken. Patients with significant history of comorbidities like CKD, congestive heart failure, nephrotic syndrome and other causes of hypoalbuminemia excluded from this study.

After collection data were edited and analyzed in a computer by using SPSS (statistical package for social science) software win version 20. Necessary statistical test like Chi-square test, t-test & correlation test (pearson/spearman) have done as per the criteria of different variable. A probability value of $p<0.05$ was considered significant.

Results:

Table-I: Gender distributions

Gender	Frequency	Percent
Female	12	24.0
Male	38	76.0
Total	50	100.0

Showing gender distributions where male was 38(76%) and female was 12(24%).

Table-11: Age group distribution-

Age	Frequency	Percent
<30 years	3	6.0
31-40 years	12	24.0
41-50 years	15	30.0
51-60 years	7	14.0
>61 years	13	26.0
Total	50	100.0

Showing age group distribution where <30 years was 3(6%), 31-40 years 12(24%), 41-50 years 15(30%), 51-60 years 7(14%) and >61 years was 13(26%).

Table-III: Occupation-

Showing occupations of the study patients where 29(58%) were doing business, house wives were 8(16%) and service holder were 13(26%)

Occupation	Frequency	Percent
Business	29	58.0
House wife	8	16.0
Service holder	13	26.0
Total	50	100.0

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Table-IV: Features of CLD-

Features	Frequency	Percent
Jaundice	19	38.0
Ascites	46	92.0
Hepatomegaly	14	24.0
Splenomegaly	36	72,0
Stigma of CLD	47	94.0

Showing different features of CLD where jaundice was present in 19(38%), hepatomegaly and splenomegaly was present in 14(24%) and 36(72%) respectively and other stigma of CLD was present in 47(94%)

Table-V: Grading of encephalopathy-

Grading	Frequency	Percent
Grade 1	15	30.0
Grade 2	9	18.0
None	26	52.0
Total	50	100.0

Showing grading of encephalopathy where Grade 1 was found in 15(30%) and Grade 2 was found in 9(18%).

Table-VI: Endoscopic grading of varices-

	Frequency	Percent
Grade 1	11	22.0
Grade 2	18	36.0
Grade 3	21	42.0
Total	50	100.0

Showing endoscopic grading where Grade 1 was found in 11(22%), Grade 2 was found in 18(36%) and Grade 3 was found in 21(42%)

Table-VII: Clinical findings-

	N	Minimum	Maximum	Mean	Std. Deviation
SBP	50	90	140	114.20	15.530
DBP	50	60	90	70.20	8.687
Valid N (list wise)					

Showing mean SBP was 140 mm of Hg and DBP was 70 mm of Hg

Table-VIII: Laboratory findings-

	N	Minimum	Maximum	Mean	Std. Deviation
Serum bilirubin	50	.50	34.70	4.5318	6.39223
Serum albumin	50	1.61	48.0	3.16	0.722
ALT (U/L)	50	16.80	246.00	64.7940	50.36999
AST(U/L)	50	4.00	342.00	61.5766	49.69857
Vitamin D3 level	50	8.00	55.70	24.2856	12.02575
PT	50	13	18	15.5	0.67
Hb%	50	9.6	16.65	10.64	3.66
TC	50	3566	12540	6544	2133

Table-IX: laboratory findings-

	Frequency	Percent
HBsAg +ve	31	62.0
Ant HBc positive	5	10.0
Anti HCV positive	4	8.0

Showing HBsAg positive case was found in 31(62%), Anti HBc positive was found in 5(10%) and Anti HCV positive was found in 4(8%) cases.

Table-X: Correlation of Vitamin D3 level with Endoscopy grading-

Endoscopy grading	Mean±SD
Grade 1(n=11)	26.8182(±16.72279)
Grade 2(n=18)	23.7150(±11.64968)
Grade 3(n=21)	23.4481(±9.72496)

Showing Grade 3 had less(23.44) Vitamin D3 then Grade 1 varices (26.818)

Table-XI: Relation of Prothrombin time with Vit D3

		PT Sec	Vitamin D3 level
PT Sec	Pearson Correlation	1	-.120
	Sig. (2-tailed)(p value)		.405
	N	50	50
Vitamin D3 level	Pearson Correlation	-.120	1
	Sig. (2-tailed) (P value)	.405	
	N	50	50

Table-XII: Relation of Vitamin D3 with ascites

Ascites	Mean	N	Std. Deviation	P value
Absent	26.2600	5	8.69126	<0.05
Present	24.0662	45	12.39731	
Total	24.2856	50	12.02575	

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Table-XIV: Correlation of Vitamin D3 level with Encephalopathy grading-

		Vitamin D3 level	Encephalopathy grading
Vitamin D3 level	Pearson Correlation	1	.177
	Sig. (2-tailed) (p value)		.218
	N	50	50
Encephalopathy grading	Pearson Correlation	.177	1
	Sig. (2-tailed) (p value)	.218	
	N	50	50

Showing weak positive correlation with Vit D3 levels and grades of encephalopathy

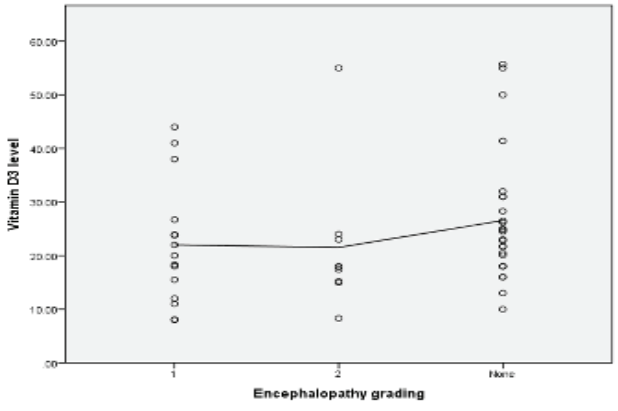

Figure 1: Correlation between Vit D3 levels and encephalopathy grading

Table XV: Correlation of Child Pugh score with Vitamin D3 level-

Child Pugh grade	Mean±SD	P value
Child Pugh A(n=4)	27.5000(±2.80357)	>0.05
Child Pugh B(n=20)	27.3605(±14.39351)	
Child Pugh C(n=26)	21.4258(±10.36024)	
Total(n=50)	24.2856(±12.02575)	

Showing correlation of Child Pugh grading with Vitamin D3 level where in CP A had mean vitamin D3 was 27.50, in CP B had 27.36 and in CP C had 21.42.

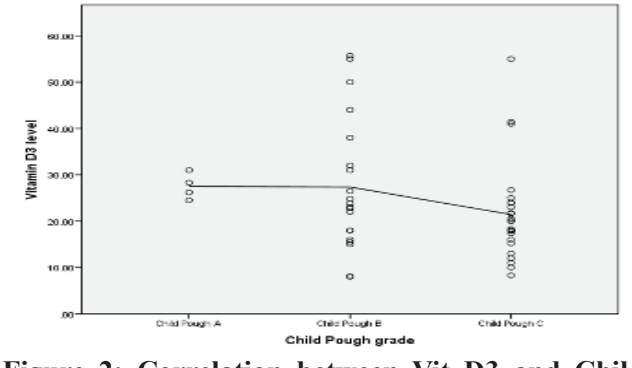

Figure 2: Correlation between Vit D3 and Child Pugh grading

Discussion:

Among 50 patients where male was 38(76%) and female was 12(24%) male to female ratio was 3.16:1. Male are more privileged person in our society and they admit in hospital more commonly then female. So this male predominant distribution is as expected. The cross-sectional study demonstrated that there was an interaction between vitamin D3 density and gender in relationship. Age group distribution revealed most patients were affected at middle age groups 31-40 years 12(24%) and 41-50 years 15(30%). From the age distribution of the patients, it was found that highest number of patients was in the age group of 41-50 years. As CLD is a chronic disease and it takes more time to make patients to be admitted so in the study most patients are middle aged. Abraldeset al.[23] had similar age group of CLD in their study. Different features of CLD were analyzed where jaundice was present in 19(38%), hepatomegaly and splenomegaly was present in 14(24%) and 36(72%) respectively and other stigma of CLD was present in 47(94%). And grading of encephalopathy revealed Grade 1 was found in 15(30%) and Grade 2 was found in 9(18%). These were found near similar done previously.[23,24]

Regarding serological and biochemical analysis HBsAg positive case was found in 31(62%), Anti HBc positive was found in 5(10%) and Anti HCV positive was found in 4(8%) cases. Serum SGPT and SGOT was also found raised in maximum patients. These findings are as expected from the patients of CLD. Correlation of Child Pugh grading with vitamin D3 level revealed in CP A had mean vitamin D3 was 27.50, in CP B had 27.36 and in CP C had 21.42. The results showed that a significant relationship was observed between Child Pugh classification and different vitamin D3 levels; on that basis, there was a trend of lower vitamin D3 level with cirrhosis increase severity. Based on the results obtained from the research, it became clear that there is a significant relationship between different vitamin D3 levels and hepatic failure severity in patients suffering from hepatic cirrhosis. On that basis, as hepatic failure severity increases, serum vitamin D3 level decrease.

Conclusion:

In conclusion there is a strong trend towards vitamin-D3 levels predicting severity in patients with cirrhosis and a low value seems to discriminate patients at higher risk for more severity. Moreover Vitamin-D3 seems to be an accurate marker of reflecting liver dysfunction and is a good synthesis-related parameter. Correlation of vitamin D3 level and CLD severity is

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found statistically significant,the clinical implication of vitamin D3 therapy in chronic liver disease may make a therapeutic benefit to the patient.

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