# Frequency of Vitamin D Deficiency in Patients with Liver Cirrhosis

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# ABSTRACT

**Objective:** To determine the frequency of vitamin D deficiency among liver cirrhosis patients and presented at Isra university hospital Hyderabad

Study design: Cross-sectional

Study setting: Gastroenterology department of Isra university Hospital, Hyderabad Sind Pakistan

Study duration: January 2018 to July 2018

All patients with age between 30 and 60 years, both genders and having evidence of cirrhosis of liver were selected in the study. Disease severity was evaluated by the Child–Pugh's classification. For the assessment of vitamin D levels, the blood samples from all patients were sent to the diagnostic laboratory. During the hospital stay and subsequent follow-up visits, the patients were monitored. All the data were collected via study proforma for the purpose of analysis.

**Results:** A total of 120 cases of liver cirrhosis were studied, their average age was 50.58+5.15 years. Males were commonest 55.0% compared to females 45.0%. Hepatitis C was the most common etiological factor 65.8%. Child–Pugh grade C was most common 57.5%. Mean of the vitamin D level was 19.16<u>+</u> 6.74 ng/ml. Almost all patients were with vitamin D deficiency as 90.0%. Vitamin D deficiency was significantly associated to the old age, HCV, alcoholic and fatty liver disease (p-<0.05), while statistically insignificant according to gender (p-0.142). **Conclusion:** It was concluded that the deficiency of vitamin D was highly prevalent 90.0%. It was significantly linked to the HCV, age and alcoholic hepatic disease.

Key words: Liver cirrhosis, vitamin D

# INTRODUCTION

The cirrhosis of the liver is a serious and incurable illness. It is a complication of chronic liver disease, which is marked by the replacement of liver tissue with fibrotic tissue and regenerative nodules, resulting in progressive hepatic function loss.<sup>1</sup> It is the most common cause of death and morbidity around the world.<sup>2</sup> In our population, it is also a common cause of death<sup>3</sup> and common cause of the Hospitals admission.<sup>4</sup> Development of the cirrhosis is about 10-20% over the period of 5-30 years. Viral hepatitis is the commonest cause compared to West the consumption of alcohol is the commonest.5 Vitamin D serves a crucial function in lowering the risk of chronic diseases, including diabetes mellitus type 2, several types of tumors, autoimmune, infectious illness and cardiovascular diseases. Among individuals with chronic liver disease (CLD), insufficiency of vitamin D is highly common. Up to 93 percent of these patients are vitamin D deficient in some way.<sup>6</sup> There is a significant hepatic role the metabolism of vitamin D and pleiotropic function. Bacterial infections, mortality, portal hypertension consequences, and fibrosis severity have all been linked to vitamin D insufficiency.<sup>6</sup> Moreover, the liver is involved pleiotropic functions and the metabolism of vitamin D, the question is whether the insufficiency of the vitamin D is a result of or a contributor to liver illness.7 severity of hepatic disease reduces vitamin D hydroxylation, DBP, and synthesis of albumin, all of which are linked to lower 25(OH)D levels. Nonetheless, vitamin D insufficiency in chronic liver disease (CLD) is only partially due to hepatic synthesis malfunction, as indicated

by the significant incidence of the deficiency of vitamin D among the non-liver cirrhosis individuals.7 Vitamin D axis has got a lot of attention in hepatic pathology because of its various features that go beyond calcium and bone homeostasis.8 Deficiency of the vitamin D id commonest among individuals with liver disorders, and preclinical research recommended that the vitamin D-based therapy may have therapeutic effects.<sup>8</sup> Several studies imply that the deficiency of the vitamin D plays the important role in the liver cirrhosis pathogenesis. Although there is a clear link between the deficiency of vitamin D and chronic liver disease and cirrhosis, while the link between deficiency of vitamin D and the development of severe hepatic fibrosis is still debated.<sup>9</sup> Vitamin D deficiency has the potential to have anti-fibrotic and the anti-inflammatory characteristics, according to certain findings.<sup>10</sup> This study aims to detect the frequency of vitamin D deficiency in patients with liver cirrhosis.

## MATERIAL AND METHODS

This cross-sectional study was conducted in department of Medicine at Isra medical university hospital Hyderabad from January 2018 to July 2018. All patients age between 30 to 60 years, diagnosed patients of liver cirrhosis and both genders were included. Individuals under the treatment of vitamin D supplement, those having incident of hepatocellular carcinoma, patients with renal failure and those who were not agreeing to participate in the study were excluded. A verbal informed consent was taken from each patient. All the patients those fulfilling the inclusion

criteria were selected in the study. All patients will carefully examine to determine the etiology of the disease. Routine lab, investigations along with ultrasound of abdomen were carried out. The severity of the condition was evaluated using a modified Child Pugh classification. The five parameters of Child-Pugh's classification is serum albumin, Prothrombin time, serum bilirubin, hepatic encephalopathy and ascites. Child Pugh class A (score less than 7), Child-Pugh class B (scoring 7-9) and Child Pugh class C (score >9).11 Furthermore, all patients' blood samples were tested for vitamin D status by quantifying serum concentration levels as 25(OH) vitamin D at the diagnostic hospital Laboratory. During their hospital stay and subsequent follow-up visits, patients were monitored. All the data was collected via study proforma for the purpose of analysis. All the data was entered and analyzed by SPSS 26.

#### RESULTS

120 patients with liver cirrhosis were included in study, mean age of patients was 50.58+5.15 years. The mean duration of liver cirrhosis was 20.13+7.89 months. Males were found in majority 55.0% and female were 45.0%. Hepatitis C was most common 65.8%, followed by hepatitis B 23.3%, alcoholic cirrhosis of liver was 3.3%, fatty liver was 6.7% and only one patient was of idiopathic. According to Child–Pugh classification, most common classification was child-Pugh grade C 57.5%, child-Pugh grade B was in 27.5% patients and child-Pugh grade A was 15.0% of the patients. Table: No. 1

Table 1: Descriptive statistics of the demographic variables n=120

Variables			
Age	Mean+SD	50.58+5.15 years	
Duration of disease	Mean+SD 20.13+7.89 Months		
Gender	Male	66(55.0%)	
	Female	54(45.0%)	
Etiology	HCV	79(65.8%)	
	HBV	28(23.3%)	
	ALCOHOL	04(3.3%)	
	FATTY LIVER	08(6.7%)	
	IDIOPATHIC	01(0.8%)	
Child Pugh class	child-Pugh grade A	18(15.0%)	
	child-Pugh grade B	33(27.5%)	
	child-Pugh grade C	69(57.5%)	

Table 2: Patients' distribution according to vitamin D deficiency  $n{=}120$ 

Vitamin D deficiency	Frequenc	
	У	Percent
Yes	108	90.0
No	12	10.0
Total	120	100.0
Mean <u>+</u> SD		19.16 <u>+</u> 6.74 ng/ml

Mean of the vitamin D level was  $19.16 \pm 6.74$ , with range of minimum 8.0 ng/ml and maximum 34.3 ng/ml. Almost all patients were with vitamin D deficiency as

90.0%, and only 10.0% patients were with sufficient level of vitamin D. Table: No. 2.

Vitamin D deficiency was found significantly associated to the old age, HCV, alcoholic and fatty liver disease (p-<0.05), while it was statically insignificant according to the gender and severity of disease (p->0.05). Table: No. 3.

Table 3. Vitamin D deficiency according to age, gender and severity of diseases n=120  $\,$ 

Variables		Vitamin D deficiency			
		Yes	No	p-value	
Age groups	30-40 years	24	8		
	41-50 years	37	3	0.003	
	51-60 years	47	1		
Gender	Male	57	9		
	Female	51	3	0.142	
Child Pugh class	child-Pugh grade A	14	4		
	child-Pugh grade B	29	4	0.105	
	child-Pugh grade C	65	4	0.105	
Etiology	HCV	74	5		
	HBV	21	7	0.047	
	Alcohol	4	0		
	Fatty liver	8	0		
	Idiopathic	1	0		

#### DISCUSSION

Vitamin D insufficiency has significant implications in chronic liver illness, including links to fibrosis severity and consequences like infections, hepatocellular cancer, and mortality.12 In this study, patient's average age was 50.58+5.15 years with range of minimum 30 years and maximum 60 years. The mean duration of liver cirrhosis was 20.13+7.89 months, with range of minimum 10 months and maximum of 41 years and males were in majority 66(55.0%). In comparison to our study, a study by Ahmad MS et al<sup>9</sup> reported that mean of the patients with CLD and deficiency of vitamin D was 52.66 years and males were commonest. Similar results were found in the study conducted by Anty R et al,13 who demonstrated that the males were in the majority. In the study of Llibre-Nieto G et al<sup>15</sup> reported that the average age of the study subjects was 62.6 ± 10.3 years, and males were in majority as 76.8%. In comparison to our results study conducted by Rahimoon AG et al<sup>15</sup> found that males were 60.0% and females were 40.0%, with the mean age of 49.8±6.5 years.

In this study, according to Child–Pugh classification, most common classification was child-Pugh grade C 57.5%, child-Pugh grade B was in 27.5% patients and child-Pugh grade A was 15.0% of the patients. On other hand, Llibre-Nieto G et al<sup>14</sup> found that the most of the patients enrolled had severe liver disease: 9.6% cases were found with Child-Pugh class A, 56% were observed with Child–Pugh class B 34.4% were seen with Child-Pugh class C. In the present series the level of vitamin D was significantly linked to the old age, HCV, alcoholic and fatty liver disease (p-<0.05). In comparison to this, a study conducted by Zubia Jamil et al<sup>16</sup> reported that in regards to the Child-Pugh class of the hepatic cirrhosis, the vitamin D insufficiency is linked to female gender, age and model of end-stage liver disease score.

In our study, almost all patients were with vitamin D deficiency as 90.0%, and only 10.0% patients were with sufficient level of vitamin D; average of the vitamin D level was 19.16+6.74 ng/ml. In comparison to this study, many comprehensive studies and trials have been documented the deficiency of vitamin D deficiency among patients of liver cirrhosis is severe. In a study of 345 individuals with liver cirrhosis, Zhao et al.17 discovered that these patients' vitamin D levels were considerably low. Fernandez et al18 discovered that 87 percent of the cirrhotic cases had a deficiency of vitamin D and in another study conducted in Spain. In another series of 160 cirrhotic individuals, Kumar et al.19 discovered that 80 percent of them had inadequate levels of the vitamin D. Vitamin D is a fat-soluble hormone that regulates bone metabolism and calcium homeostasis, but it also seems to have a role in fibrogenesis in the liver. Sunlight exposure, certain items in the diet, and some health supplements are all sources of vitamin D. The link of the hepatic function, fibrosis severity, and infection consequences with the vitamin D deficiency, may justify its use as the diagnostic tool and as a prognostic index. In vast prospective cohort reports and randomized trials, the effect of the deficiency of vitamin D in patients of liver cirrhosis needs to be investigated and proven further.<sup>20</sup>

## CONCLUSION

It was concluded that the vitamin D deficiency highly prevalent (90.0%) among patients of liver cirrhosis. It is commonly observed in HCV-infected and alcoholic liver disease patients. The patients of the hepatic disease should take the vitamin D supplement and eat foods high in vitamin D. Gastroenterologists should screening of vitamin D levels in patients presented with chronic liver disease, to decrease early cirrhosis by its management. Further large-scale studies should be done on this event.

## REFERENCES

- Gildea TR, Cook WC, Nelson DR, Aggarwal A, Carey W, Younossi ZM. Predictors of long-term mortality in patients with cirrhosis of the liver admitted to a medical ICU. Am Coll Chest Physicians 2004;126:1598-603.
- Almani SA, Memon AS, Memon AI, Shah I, Rahpoto Q, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. J Liaquat Uni Med Health Sci. 2008 May;7(2):61-.
- Nadeem MA, Waseem T, Sheikh AM, Grumman N, Irfan K, Hasnain SS. Hepatitis C virus: An alarmingly increasing cause of liver cirrhosis in Pakistan. Pak J Gastroenterol 2002;16(1):3-8.
- Hussain I, Nasrullah M, Shah AA. Prevalence of hepatitis B and C viral infections in liver cirrhosis in Pakistan. Pak J Gastroenterol 1998;12(1-2):7-11.
- Khan MA, Dar HA, Baba MA, Shah AH, Singh B, Shiekh NA. Impact of vitamin D status in chronic liver disease. Journal of

clinical and experimental hepatology. 2019 Sep 1;9(5):574-80.

- Iruzubieta P, Terán Á, Crespo J, Fábrega E. Vitamin D deficiency in chronic liver disease. WJH 2014 Dec 27;6(12):901.
- Elangovan H, Chahal S, Gunton JE. Vitamin D in liver disease: Current evidence and potential directions. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2017;1;1863(4):907-16.
- Ahmad MS, Dawood N, Abaidullah S, Nazim R, Iqbal S. Correlation Between Vitamin D Deficiency and Severity of Liver Disease among Cirrhotic Patients. Annals of King Edward Medical University. 2021 Nov 4;27(Special Issue (Jul-Sep)):362-7.
- Jha AK, Jha SK, Kumar A, Dayal VM, Jha SK. Effect of replenishment of vitamin D on survival in patients with decompensated liver cirrhosis: A prospective study. World J Gastrointest Pathophysiol 2017; 8(3): 133-141
- Lange CM, Bojunga J, Ramos-Lopez E, von Wagner M, Hassler A, Vermehren J et al. Vitamin D deficiency and a CYP27B1-1260 promoter polymorphism are associated with chronic hepatitis C and poor response to interferon-alfa based therapy. J Hepatol 2011;54:887-93
- 11. Koop AH, Mousa OY, Pham LE, Corral-Hurtado JE, Pungpapong S, Keaveny AP. An argument for Vitamin D, A, and zinc monitoring in cirrhosis. Annals of hepatology. 2018 Nov 1;17(6):920-32.
- Anty R, Tonohouan M, Ferrari-Panaia P, Piche T, Pariente A, Anstee QM et al. Low Levels of 25-Hydroxy Vitamin D are Independently Associated with the Risk of Bacterial Infection in Cirrhotic Patients. *Clin Transl Gastroenterol* 2014;5:e56
- Llibre-Nieto G, Lira A, Vergara M, Solé C, Casas M, Puig-Diví V, Solé G, Humanes A, Grau L, Barradas JM, Miquel M. Micronutrient Deficiencies in Patients with Decompensated Liver Cirrhosis. Nutrients. 2021 Apr;13(4):1249.
- Rahimoon AG, Maheshwari SD, Memon N. Chronic liver disease; vitamin D deficiency in the patients. Professional Med J 2015;22(7):844-848.
- Jamil Z, Arif S, Khan A, Durrani AA, Yaqoob N. Vitamin D Deficiency and Its Relationship with Child-Pugh Class in Patients with Chronic Liver Disease. JCTH. 2018 Feb 1;6(2):1-6.1
- Zhao XY, LiJ, Wang JH ,Habib S, Wei W, Sun SJ, et al. Vitamin D serum levelis associated with Child-Pugh score and metabolic enzyme imbalances, but not viral load in chronic hepatitis B patients. Medicine (Baltimore) 2016;95: e3926.
- Fernández NF, Torres PL, Matias DJ, Plaza FJ, Goñi JL. Vitamin D deficiency in chronic liver disease, clinicalepidemiological analysis and report after vitamin d supplementation. Gastroenterología y Hepatología (English Edition). 2016 May 1;39(5):305-10.
- KumarŔ,KumarP, Saxena KN,Mishra M,Mishra VK, Kumari A,etal.VitaminD status in patients with cirrhosis of the liver and their relatives-A case control study from North India. Indian J Gastroenterol 2017;36:50–55.
- Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology. 2016 Jul;29(3):297.