



ASSOCIATION OF SERUM CALCIUM, SERUM PHOSPHATE AND SERUM VITAMIN D WITH SEVERITY OF CHRONIC LIVER DISEASE

General Medicine

Shiv Ghodasara

Y N Verma

ABSTRACT

Background: Chronic liver disease (CLD) is characterized by continuous decline in hepatic performance for over 6 months, that involves generation of coagulation factors, several other proteins, elimination of dangerous metabolic byproducts as well as bile elimination. In CLD, the serum phosphate concentrations change. According to the majority of research, it generally results in hypophosphatemia. It can have a variety of explanations, including internal rearrangement, reduced uptake, as well as excessive elimination. There is a connection between the metabolic activities of serum calcium, phosphate, as well as vitamin D. Comparatively fewer investigations have been conducted in subjects with CLD. Therefore, it is necessary to link or associate each of these to people who have CLD. **Method:** In this study, a total of 60 patients diagnosed with chronic liver disease were taken over a period of 6 months (Jan to June 2022). All relevant data were recorded and analyzed. **Results:** Among 60 patients, 45 percent of the patients belonged to the age group of 41 to 50 years. 78.33 percent of the patients were males while the remaining were females. Mean serum vitamin D levels, serum calcium and phosphate levels were found to be 23.42 ng/mL, 8.67 mg/dL and 3.12 mg/dL respectively. **Conclusion:** Vitamin D deficiency is documented in the majority of patients afflicted by CLD, particularly those having advanced disease. As the disease advances, the levels become lesser. However, serum calcium and phosphate levels doesn't show any significant correlation with severity of disease.

KEYWORDS

INTRODUCTION

Chronic liver disease (CLD) is characterized by continuous decline in hepatic performance for over 6 months, that involves generation of coagulation factors, several other proteins, elimination of dangerous metabolic byproducts as well as bile elimination. It seems to be a progressive procedure of swelling, degradation as well as renewal of hepatic parenchyma, that results in fibrosis as well as cirrhosis. Cirrhosis is the end stage of CLD which leads to degradation of hepatic structure, the production of nodules, vascular re-establishment, the production of new blood vessels from pre existing ones as well as accumulation of ECM (extracellular matrix)¹⁻⁴

Phosphorus as well as calcium absorption are linked. When blood calcium concentrations increase, phosphate concentrations decrease inside the body, which is the reverse of how calcium as well as phosphate interact. The amounts of calcium and phosphorus within our blood are controlled by parathyroid hormone. A few illnesses or infections have the potential to alter the relationship among calcium as well as phosphate. Because of this, calcium as well as phosphate concentrations are frequently determined together.⁵⁻⁷

The frequency of vitamin D deficiency is substantially greater amongst CLD sufferers. Nearly 1/3rd of people having CLD exhibit significant vitamin D shortage, whereas upto ninety three percent of such individuals possess low vitamin D concentrations.⁸

There is a connection between the metabolic activities of serum calcium, phosphate, as well as vitamin D. Therefore, it is necessary to link or associate each of these to people who have CLD. A popular grading methodology for predicting the 1-year rate of survival of cirrhotic subjects has been the Child-Pugh score.

This score, which was initially proposed by Child & Turcotte as well as subsequently revised by Pugh et al., incorporates 5 specifications to categorise subjects, namely hepatic encephalopathy, prothrombin time, ascites, serum bilirubin, as well as serum albumin.⁸⁻¹¹

CHILD-PUGH SCORE

Clinical lab criteria	Points-1	2	3
Encephalopathy	None	Grade 1 or 2	Grade 3 or 4
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin(mg/dl)	<2	2-3	>3
Albumin	>3.5	2.8-3.5	<2.8
PT(INR)	<4/1.7	4/1.7 – 6/2.3	>6/2.3

AIMS & OBJECTIVES

Aim:

To study the correlation of the levels of calcium, phosphate and vitamin D with severity of chronic liver disease patients.

Objectives:

- To study clinical and etiological profile of chronic liver disease patients.
- To assess the level of serum calcium, serum phosphate and serum vitamin D in patients of chronic liver disease.
- To study the correlation between calcium, phosphate and vitamin D with severity of chronic liver disease using the Child-Pugh score.

MATERIALS AND METHODS :-

This was an observational study and will be conducted on patients with diagnosis of chronic liver disease presented at Geetanjali Medical College and Hospital, Udaipur. Detailed history and detailed clinical examination was done. Serum. Calcium, serum phosphate, vitamin D3, liver function test was done. PT(INR), Ultrasonography.

OBSERVATIONS AND RESULTS :

Table 1: Age And Gender-wise Distribution Of Patients

Age group (years)	Number of patients	Percentage
18 to 30	3	5
31 to 40	14	23.33
41 to 50	27	45
51 to 60	9	15
More than 60	7	11.67
Total	60	100
Mean $\pm$ SD	47.23 $\pm$ 11.16	
Gender	Number of patients	Percentage
Males	47	78.33
Females	12	21.67

The present study was conducted for association of serum calcium, serum phosphate, serum vitamin D with severity of chronic liver disease in 60 patients at Geetanjali Medical College and Hospital, Udaipur. Following results were obtained:

- 45 percent of the patients belonged to the age group of 41 to 50 years while 23.33 percent of the patients belonged to the age group of 31 to 40 years. Mean age of the patients was 47.23 years. (Table 1)
- Out of 60 patients, 78.33 percent of the patients were males while the remaining were females. (Table 2)
- Mean vitamin D levels among the patients with Child-Pugh Class A, class B and class C was 29.47 ng/ml, 23.99 ng/ml and 14.24 ng/ml respectively. On analyzing statistically, it was seen that vitamin D levels showed significant reduction with increasing severity of CLD as assessed by Child-Pugh score (p-value < 0.05)

- Mean calcium levels among the patients with Child-Pugh Class A, class B and class C was 8.65 mg/dL, 8.67 mg/dL and 8.68 mg/dL respectively. On analyzing and comparing statistically, no significant correlation of serum calcium was observed with severity of CLD as assessed by Child-Pugh score (p -value > 0.05).
- Mean phosphate levels among the patients with Child-Pugh Class A, class B and class C was 3.12 mg/dL, 3.17 mg/dL and 2.98 mg/dL respectively. On analyzing and comparing statistically, no significant correlation of serum phosphate was observed with severity of CLD as assessed by Child-Pugh score (p -value > 0.05).

Table 2: Serum Vitamin D, Calcium And Phosphate Levels (mean Levels)

Variables	Mean	SD
Serum Vitamin D levels (ng/mL)	23.42	7.62
Serum calcium levels (mg/dL)	8.67	0.54
Serum phosphate levels (mg/dL)	3.12	0.52

Table 3: Correlation of Vitamin D levels with Child-Pugh Score

Child-Pugh Score	Mean	SD	p- value
Grade A	29.47	7.41	0.000
Grade B	23.99	5.77	(Significant)
Grade C	14.24	1.32	

Table 4: Correlation Of Serum Calcium Levels With Child-pugh Score

Child-Pugh Score	Mean	SD	p- value
Grade A	8.65	0.59	0.1180
Grade B	8.67	0.53	
Grade C	8.68	0.54	

Table 5: Correlation Of Serum Phosphate Levels With Child-pugh Score

Child-Pugh Score	Mean	SD	p- value
Grade A	3.12	0.63	0.2171
Grade B	3.17	0.52	
Grade C	2.98	0.43	

DISCUSSION

Chronic liver disorders (CLD) are a major source of illness and mortality. In CLDs, a variety of etiological variables result in a comparable clinico-pathological condition, however the rates of development and clinical trajectory may vary. There was a forty six percent rise in CLD mortality globally (1980-2013), highlighting the disease's growing public health significance¹²⁻¹⁴

In our study, a total of 60 patients were analyzed. 45 percent of the patients belonged to the age group of 41 to 50 years while 23.33 percent of the patients belonged to the age group of 31 to 40 years. Mean age of the patients was 47.2 years.

Mukherjee PS et al who also reported similar findings. In their nationwide Indian study, mean age of the patients was 42.8 years. Among them, mean age of the patients of Northern region, Eastern region, Southern region, Western region and central region of Indian subcontinent was 41.1 years, 41.7 years, 43 years, 46.3 years and 46.3 years respectively.¹⁵

Jamil et al, in their study reported the mean age of the patients with CLD to be 56.88 years.¹⁶

In a study conducted by Patel JK et al, most of patients (57%) were between the age of 31 to 50 years. The youngest cirrhotic was 22 years, the oldest being 65 years. The mean age of cases was 42.92 years.¹⁷

In another study conducted by J. Arteh et al, mean age of the patients was 53 years.¹⁸ Our findings were in concordance with the results obtained by the above studies.

In our study, out of 60 patients, 78.33 percent of the patients were males while the remaining were females.

In a study conducted by Mallik S et al, 68.57 percent of the patients were males while the remaining were females.²²

In the study conducted by Patel JK et al, 77 percent of the patients were males and remaining 23 percent were females.¹⁷

Our results were in concordance with the results obtained by previous

authors who also reported male preponderance in their respective studies.

In our study, mean vitamin D levels among the patients with Child-Pugh class A, class B and class C was 29.47 ng/ml, 23.99 ng/ml and 14.24 ng/ml respectively. On analyzing statistically, it was seen that vitamin D levels showed significant reduction with increasing severity of CLD as assessed by CP score (p -value < 0.05).

In a study conducted by Patel JK et al, the mean vitamin D level was 20.91 with Child-Pugh Class A ($n=22$), 16.43 with Child-Pugh Class B ($n=53$) and 10.66 with Child-Pugh Class C ($n=25$). There was consistent trend towards lower vitamin D level with increasing severity of cirrhosis. Vitamin D level showed significant negative correlation with Child-Pugh score.¹⁷

Zhao et al conducted a study on 345 cirrhotic patients and found that vitamin D levels were significantly deficient in these patients.²⁰

Thus, patients with higher scores in the Child-Pugh 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. Our result was in concordance with the results obtained by previous authors who also reported similar findings regarding the mean vitamin D levels with that of child-pugh score

In our study, mean calcium levels among the patients with Child-Pugh class A, class B and class C was 8.65 mg/dL, 8.67 mg/dL and 8.68 mg/dL respectively. On analyzing and comparing statistically, no significant correlation of serum calcium was observed with severity of CLD as assessed by Child-Pugh score (p -value > 0.05).

In a study conducted by Miroliaee et al, mean calcium levels among CLD patients with Child-Pugh class A and B combined was 8.84 mg/dL and Child-Pugh Class C was 8.21 mg/dL respectively. They also observed no significant correlation of serum calcium was observed with severity of CLD as assessed by Child-Pugh score.²¹

Our results were in concordance with the results obtained by previous authors who also reported similar findings.

In our study, mean phosphate levels among the patients with Child-Pugh class A, class B and class C was 3.12 mg/dL, 3.17 mg/dL and 2.98 mg/dL respectively. On analyzing and comparing statistically, no significant correlation of serum phosphate was observed with severity of CLD as assessed by Child-Pugh score (p -value > 0.05).

In a study conducted by Miroliaee et al, mean calcium levels among CLD patients with Child-Pugh class A and B combined was 3.03 mg/dL and Child-Pugh Class C 3.13 mg/dL respectively. They also observed no significant correlation of serum calcium was observed with severity of CLD as assessed by Child-Pugh score (p -value > 0.05).²¹

CONCLUSION

Vitamin D deficiency is documented in the majority of patients afflicted by CLD, particularly those having advanced disease. As the disease advances, the levels become lesser. However, serum calcium and phosphate levels doesn't show any significant correlation with severity of disease. Vitamin D levels should be routinely checked in all patients suffering from advanced CLD, so that adequate replacement by vitamin D supplements can be initiated as a therapeutic adjunct in managing such patients.

REFERENCES:

1. Heidebaugh JJ, Brudery M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician. 2006 Sep 01;74(5):756-62.
2. Poynard T, Mathurin P, Lai CL, Guyader D, Poupon R, Tainturier MH, Myers RP, Muntenau M, Ratzu V, Manns M, Vogel A, Capron F, Chedid A, Bedossa P, PANFIBROSIS Group. A comparison of fibrosis progression in chronic liver diseases. J Hepatol. 2003 Mar;38(3):257-65.
3. Bataller R, North KE, Brenner DA. Genetic polymorphisms and the progression of liver fibrosis: a critical appraisal. Hepatology. 2003 Mar;37(3):493-503.
4. Tsuchida T, Friedman SL. Mechanisms of hepatic stellate cell activation. Nat Rev Gastroenterol Hepatol. 2017 Jul;14(7):397-411.
5. Sepanlou SG, Safiri S, Bisignano C, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 2020; 5: 245-266.
6. Mokdad AA, Lopez AD, Shahrz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med 2014; 12: 145.
7. Konstantakis C, Tselekiou P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. Ann Gastroenterol. 2016;29(3):297-306.

8. Cheemerla S, Balakrishnan M. Global Epidemiology of Chronic Liver Disease. *Clinical liver diseases*. 2021; 17(5): 365-370.
9. Sepanlou SG, Safiri S, Bisignano C, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol* 2020; 5: 245-266.
10. Mokdad AA, Lopez AD, Shahrzaz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med* 2014; 12: 145.
11. Konstantakis C, Tselekouni P, Kalafateli M, Triantos C. Vitamin D deficiency in patients with liver cirrhosis. *Ann Gastroenterol*. 2016;29(3):297-306.
12. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357:266–281.
13. Holick MF. Vitamin D: evolutionary, physiological and health perspectives. *Curr Drug Targets*. 2011;12:4–18.
14. Looker AC, Dawson-Hughes B, Calvo MS, Gunter EW, Sahyoun NR. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. *Bone*. 2002;30:771–777
15. Mukherjee, P. S., Vishnubhatla, S., Amarapurkar, D. N., Das, K., Sood, A., Chawla, Y. K et al. Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. *PloS one*, 2017; 12(10): e0187033.
16. 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. *J Clin Transl Hepatol*. 2018;6(2):135-140.
17. Patel JK, Mahur HK, Jat SS, Singh DP. A study of the correlation of serum vitamin D levels to Child-Pugh and MELD-Na scoring system in cirrhosis of the liver. *Int J Res Med Sci* 2021;9:210-5.
18. Arteh J, Narra S, Nair S. Prevalence of vitamin D deficiency in chronic liver disease. *Digestive diseases and sciences*. 2010 Sep;55(9):2624-8.
19. Kiani IG, Shah F, Mansur SS. Frequency of severe vitamin-D deficiency in patients presenting to a tertiary care hospital in Islamabad. *J Pak Med Assoc* 2014;64:1138–1140
20. Zhao XY, Li J, Wang JH, Habib S, Wei W, Sun SJ, et al. Vitamin D serum level is associated with Child-Pugh score and metabolic enzyme imbalances, but not viral load in chronic hepatitis B patients. *Medicine (Baltimore)* 2016;95: e3926
21. Miroliaee A, Nasiri-Toosi M, Khalilzadeh O, Esteghamati A, Abdollahi A, Mazloumi M. Disturbances of parathyroid hormone–vitamin D axis in noncholestatic chronic liver disease: a cross-sectional study. *Hepatology international*. 2010 Sep;4(3):634-40.
22. Mallik S, Sarkar K, Rahman M, Halder SN. Clinical and etiological study on chronic liver diseases. *International Journal of Contemporary Medicine Surgery and Radiology*. 2018;3(2):B77-B80.