

Original article:

Association of vitamin-D levels with the severity of liver disease

Jayagowri Karthikeyan, Sujatha Rajaragupathy

Department of Biochemistry, PSG Institute of medical sciences and research , Coimbatore 641004

Corresponding author: Sujatha Rajaragupathy

Department of Biochemistry, PSG Institute of medical sciences and research, Coimbatore 641004

ABSTRACT

INTRODUCTION: Chronic liver diseases (CLD) are characterized by liver injury, chronic inflammation and finally by progressive substitution of liver parenchyma by scar tissue. Vitamin-D insufficiency and deficiency are prevalent in almost half the healthy population of developed countries. The scores used to assess the prognosis of CLD are the Child-Pugh (CP) score and the Model for end-stage liver disease (MELD) score. To understand the relationship between vitamin-D levels and prognosis of CLD, it has to be compared with prognostic scores like CP and MELD. The objective of this study is to compare the levels of vitamin-D with the severity scores of liver disease like Child-Pugh (CP) score and Model for End-stage Liver Disease (MELD).

METHOD: After obtaining approval of human ethics committee, in a sample size of 100 CLD patients, data such as age, gender, etiology of CLD, vitamin-D, CP score, MELD score, and liver function tests were obtained. Data was entered in Microsoft Excel. Analysis was done and expressed in Mean \pm SD, percentages and frequencies.

OBSERVATION AND RESULTS: A total of 100 chronic liver disease patients of various etiologies were included in the study, out of which 88% were males. The mean age group of the subjects was 50.36 \pm 20.48 years. Among the study population, 91% had low vitamin D levels. 56% of the cases were alcoholic liver disease and the remaining etiologies included NAFLD, Viral, autoimmune and others. Among the vitamin D deficient cases (n=82), 56 belong to the Child Pugh-C score (45% of one year survival). There was no significant correlation between the MELD score and vitamin-D levels in the study population.

CONCLUSION: It is found that patients with very low vitamin-D levels had the worst prognosis measured using Child Pugh score. Maintenance of normal vitamin-D levels will provide a better prognosis and a better quality of life for CLD patients under treatment.

KEYWORDS: vitamin-D, liver disease, severity

INTRODUCTION:

Vitamin-D is a fat-soluble vitamin which plays a major role in calcium metabolism. Its need is satisfied by diet as well as absorption through skin. Due to decrease in vitamin-rich diet and sunlight exposure, vitamin-D deficiency occurs. Vitamin-D insufficiency and deficiency are prevalent in almost half the healthy population of developed countries.⁽¹⁾ It is estimated that one billion people suffer from deficiency or insufficiency of vitamin-

D.⁽²⁾ The impact of this deficiency is seen not only in bones but also in other organs which were not investigated until recently. Recent studies are done to assess the influence of vitamin-D deficiency in the progression of various diseases. Chronic liver diseases (CLD) are characterized by liver injury, chronic inflammation and finally by progressive substitution of liver parenchyma by scar tissue. It includes a plethora of diseases ranging from alcoholic liver disease, non-alcoholic fatty liver

disease till metabolic diseases like Wilson's disease. In patients with CLD, the prevalence of vitamin-D deficits is much higher and practically universal.⁽³⁾ Up to 93% of patients with chronic liver disease have insufficient vitamin-D levels, and almost one-third of them show severe deficiency.⁽⁴⁾ This is attributed to the poor secretion of bile which is needed for the absorption of this fat-soluble vitamin. Vitamin-D deficiency has been associated with liver disease progression and its supplementation has been suggested as a treatment to prevent progression of disease.⁽⁵⁾ The scores used to assess the prognosis of CLD are the Child-Pugh (CP) score and the Model for end-stage liver disease (MELD) score. The Child Pugh (CP) score is calculated using the parameters Total Bilirubin, Serum Albumin, PT-INR, Ascites and Hepatic Encephalopathy. According to CP scores, class A indicates 100% one year survival while class C indicates 45% one year survival. The MELD score is calculated using serum creatinine, bilirubin and PT-INR. To understand the relationship between vitamin-D levels and prognosis of CLD, it has to be compared with prognostic scores like CP and MELD. Data on the association of vitamin-D status with prognostic parameters for liver dysfunction, such as the Child-Pugh (CP) score and the model for end-stage liver disease (MELD) score are sparse. The association between vitamin-D levels and these scores indicates the role of vitamin-D in the severity of the disease.

AIMS AND OBJECTIVES:

The main objective of this study is to evaluate the vitamin-D status of patients with chronic liver

disease and establish an association with the severity of the disease. To achieve this aim, we compared the levels of vitamin-D with the severity scores of liver disease like Child-Pugh (CP) score and Model for End-stage Liver Disease (MELD).

MATERIAL AND METHODS:

This retrospective study was conducted in a tertiary care centre in south India. After obtaining approval from the Institutional Human Ethics Committee, patients with CLD attending the gastroenterology and medicine outpatient and inpatient department in our hospital over a period of one year were included in the study. Patients in whom vitamin-D levels were not estimated were excluded from the study. In a sample size of 100 patients, data such as age, gender, etiology of CLD, vitamin-D, CP score, MELD score, and liver function tests of the participants were obtained from medical records.

Lips classification states that vitamin-D level of more than or equal to 30ng/ml is considered normal, 20-29.9 ng/ml is considered insufficiency and less than 20 ng/ml is considered as deficient.⁽⁶⁾ Data collected was anonymized by removing direct identifiers. Data was entered in Microsoft Excel. Analysis was done and expressed in Mean±SD, percentages and frequencies.

OBSERVATIONS AND RESULTS:

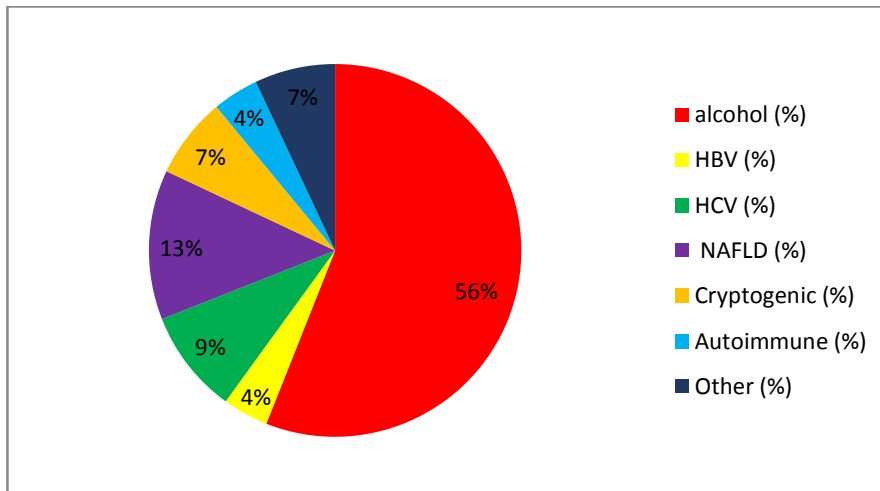
Among a total of 512 chronic liver disease cases, 100 of them had their vitamin-D levels estimated and were included in the study. The average age of the study population was 50.3 ± 10.2 years and 88% of them were males. Baseline characteristics of the study population are listed in Table 1.

Table 1: Baseline characteristics of study group

Age	50.36±10.24
Gender	Males: 88 Females:12
LFT mean values	Total bilirubin: 6.9 mg/dL ALT: 34.5 U/L AST:69.8 U/L ALP: 131.4 U/L GGT: 18.2 U/L Albumin 2.6 g/dL

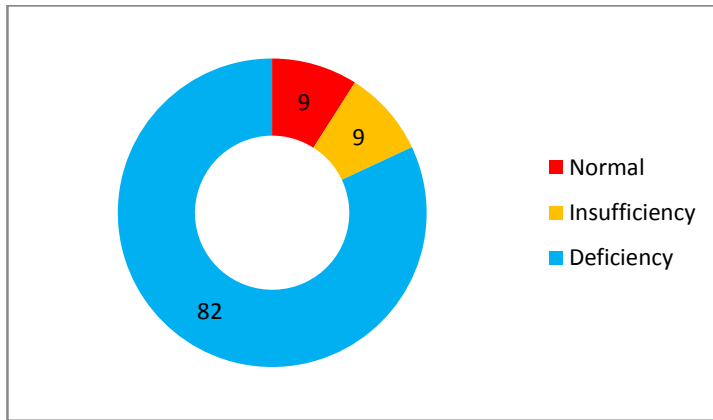
The etiology for liver disease in the study group ranged from alcohol, viral (Hepatitis B, C) to autoimmune. The findings are displayed in Figure 1.

Figure 1: Etiology of CLD in the study population



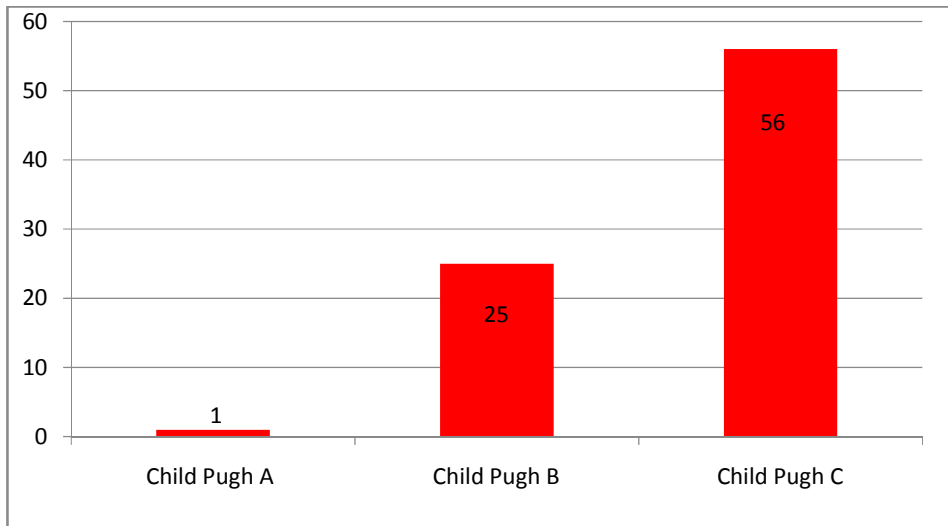
The serum vitamin-D levels in the participants were analysed. It was found that nearly 82% of the CLD patients had insufficient or deficient vitamin-D levels. (Figure 2)

Figure2: Vitamin-D status in the study population



Among the vitamin-D deficient individuals with CLD, CP score was compared and it was found that 56 (68.3%) were in the child pugh C score. (Figure 3)

Figure 3: Association of child-pugh score and vitamin-D levels



Comparison of MELD scores showed that 71 (86.5%) of vitamin-D deficient cases had MELD score of less than 30.

DISCUSSION:

Studies done to correlate vitamin-D deficiency with the severity of CLD using scores like CP and MELD are few. In this study, majority of the subjects (88%) were males. This finding was not consistent with other studies done by Putz-Banktiet al (68%) and Barchettaet al (52%).^(6,7) Higher

propotion of the study population had alcohol as the cause of CLD. This was similar with the findings of study by Putz-Banktiet al but a study by Arthet al showed HCV as the cause of CLD.^(6,4) Higher population of males could be attributed to the primary etiology being alcohol-induced.

In this study, the prevalence of vitamin-D deficiency is 82% while the study by Arthet al showed a prevalence of 64-92%.⁽⁴⁾ According to this study results, CP score C contains more number of vitamin-D deficient cases than class A or class B. A similar result was seen in a study by Fisher et al in which vitamin-D deficient cases were highly found in class C.⁽⁸⁾ This study did not show significant correlation between vitamin-D levels but MELD score while the study by Putz-Banktiet al showed inverse correlation between MELD score and vitamin-D levels.

In CLD, vitamin-D deficiency is observed due to various reasons. The absorption of this fat-soluble vitamin requires bile, produced by the liver. The activation of vitamin-D requires 25-hydroxylase enzyme, which is present only in the liver cells. Though vitamin-D metabolism is closely associated to liver, whether vitamin-D deficiency influences the prognosis of CLD is still to be evaluated. This study serves to form a platform for future research

on vitamin-D deficiency and CLD. This study will help physicians to understand that maintaining normal vitamin-D levels will provide a better prognosis and a better quality of life for CLD patients under treatment.

The main limitation of the study is the sample size. A larger study population is essential for better results.

CONCLUSION:

Greater proportions of poor-prognostic liver disease patients have low vitamin-D levels. Low vitamin-D levels could be a hinderance for the recovery of CLD patients.

The future scope of this study is that it can be carried out as a case-control study and interventional study. Clinical drug trials can be conducted to confirm the influence of normal vitamin-D levels in retarding the progression of CLD.

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