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A study of serum levels of magnesium, calcium and vitamin-d in alcoholic liver disease patients in a tertiary care hospital in Goa: A case control study

1Dr. Saiesh M. Mardolkar, Department of Biochemistry, Goa Medical College and Hospital, Bambolim, 403202, India.

<sup>1</sup>Dr. Chitra Y. Dhume, Department of Biochemistry, Goa Medical College and Hospital, Bambolim,403202, India.

<sup>2</sup>Dr. Megha Goel, Department of Biochemistry, Goa Medical College and Hospital, Bambolim,403202, India.

<sup>3</sup>Dr. Abhishek Bicholkar, Department of Preventive and Social Medicine, Goa Medical College and Hospital, Bambolim, 403202, India.

**Corresponding Author:** Dr. Saiesh M. Mardolkar, Department of Biochemistry, Goa Medical College and Hospital, Bambolim,403202, India.

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# Abstract

Alcohol consumption has shown multiple adverse consequences on practically every organ system in the human body with the most devastating being alcoholic liver cirrhosis. Patients consuming excessive amounts of alcohol are prone to various micronutrient deficiencies, protein-calorie malnutrition and electrolyte disturbances. Chronic alcohol consuming patients are malnourished not only because of poor nutrition but also due to impaired absorption of essential micronutrients. In Goa, liver disease caused by alcohol consumption was responsible for 10 - 11% of all deaths registered at Goa Medical College reported in 2013. The current study is aimed at assessing serum levels of magnesium, calcium and vitamin D among patients with alcoholic liver

disease and to compare these levels with those without liver disease.

A Case-control study was conducted on newly admitted patients of alcoholic liver disease in the General Medicine wards of Goa Medical College. After taking written consent, 60 patients with alcoholic liver disease diagnosed based on clinical and radiological evidence were included as cases. Whereas 60 patients admitted in same wards without liver disease were included in the study as control after taking consent. The biochemical investigations of the patients and socio-demographic details were collected on the first day of admission. The data was analysed using SPSS version 14.

The mean age among the cases was  $47.52 \pm 11.5$  years. The mean age among the controls is  $51.6 \pm 12.95$  years. The mean levels of serum magnesium, serum calcium and serum vitamin D among the cases are  $1.67 \pm 0.29$ mg/dl,  $7.39 \pm 0.66$  mg/dl and  $9.34 \pm 7.91$  ng/ml respectively. Whereas for controls they are  $2.1 \pm 0.33$ mg/dl,  $9.3 \pm 0.36$  mg/dl and  $26.37 \pm 6.9$  ng/ml respectively. There is a statistically significant difference in mean levels of serum magnesium, serum calcium and vitamin D levels across the cases and controls group.

**Keywords:** Alcohol, cirrhosis, liver, magnesium, calcium, vitamin D

## Introduction

Alcohol consumption has been shown to have multiple adverse consequences on practically every organ system in the human body with the most devastating being alcoholic liver cirrhosis. Alcoholic liver disease is manifested as a spectrum of disorders with progressive injury ranging from fatty liver, alcoholic hepatitis, cirrhosis and superimposed hepatocellular carcinoma.<sup>[1]</sup> Alcohol is the world's third largest risk factor for disease burden. The harmful use of alcohol results in about 3.5 million deaths worldwide each year.<sup>[2]</sup>In Goa, liver disease caused by alcohol consumption was responsible for 10 - 11% of all deaths registered at Goa Medical College reported in 2013.<sup>[3]</sup>

Patients consuming excessive amounts of alcohol are prone to various micronutrient deficiencies, proteincalorie malnutrition as well as electrolyte disturbances. Chronic alcohol consuming patients are malnourished not only because of poor nutrition but also due to impaired absorption of essential micronutrients.

Magnesium, which is the 2<sup>nd</sup> most common intracellular cation is involved in many biological functions which include DNA replication and repair, intermediary metabolism, ion transport, cell growth and signaling pathways.<sup>[4]</sup>Studies have reported that hypomagnesemia

is a risk factor in the progression of alcoholic liver disease and is also associated with an increased risk of mortality particularly in alcohol drinkers with hepatic steatosis.<sup>[5,6]</sup>

Chronic alcohol consumption is shown to cause vitamin D deficiency and reduced absorption of calcium from intestine which predisposes to osteopenia and osteoporosis. Studies have shown that low vitamin D levels are linked to greater liver damage and mortality. Vitamin D may serve as a biomarker of severity of alcoholic liver disease as well as a possible treatment target.<sup>[7]</sup>

In our study, we assess the levels of serum magnesium, serum calcium and serum vitamin D in alcoholic liver diseases patients and compare these with patients without alcoholic liver disease.

## Aims & Objective

To assess serum levels of magnesium, calcium and vitamin D among patients with alcoholic liver disease and to compare these levels with those without liver disease.

# **Materials and Methods**

The present Case Control study was conducted in Goa Medical College and Hospital which is a tertiary care hospital in Goa. The cases comprised of patients with alcoholic liver disease in the age group of 20 - 80 years who were newly diagnosed with alcoholic liver disease based on clinical, radiological and biochemical evidence and admitted in General Medicine wards of Goa Medical College during the study period. The data collection was done over a period of 4 months from August 2022 to December 2022. The protocol of the study was approved by the Institutional Ethical Committee (IEC) prior to the start of the study. An informed consent was obtained from all the study participants who met the inclusion

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criteria and who were willing to participate in the study. Non consenting individuals were excluded from the study. Age and sex-matched controls were selected in the ratio 1:1 from the same wards without liver disease after taking consent.

Patients with non-alcoholic cause of liver disease, those diagnosed with pancreatitis and on treatment and patients on drugs interfering with the study parameters were excluded from the study.

The blood sample was collected in the wards in a plain bulb and the serum magnesium, calcium and vitamin D levels were done in OPD-13 of Department of Biochemistry in Goa Medical College using the Abbott Architect c8200i autoanalyser.

There is no conflict of interest or external source of funding.

## Results

A total of 60 patients with alcoholic liver disease which fit the inclusion criteria were included in the study. Whereas 60 age and sex matched patients without any liver disease were recruited as controls for the study. The mean age among the cases and controls is  $47.52 \pm 11.5$ years and  $51.6 \pm 12.95$  years respectively. All cases and controls are males.

Table 1: Serum Magnesium, Serum Calcium and SerumVitamin D levels in cases and controls

Parameters		N	$Mean \pm SD$	p value
Serum Magnesium	Cases	60	$1.67 \pm 0.29 \text{ mg/dl}$	<0.001
	Controls	60	2.1 ± 0.33 mg/dl	
Serum Calcium	Cases	60	7.39 ± 0.66 mg/dl	<0.001
	Controls	60	9.31 ± 0.36 mg/dl	
Serum Vitamin D	Cases	60	9.34 ± 7.91 ng/ml	<0.001
	Controls	60	26.37 ± 6.9 ng/ml	

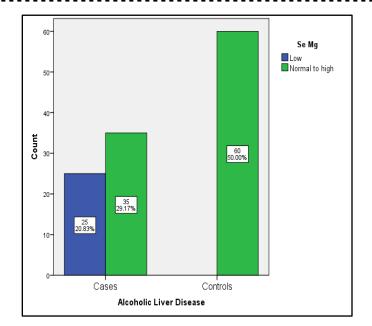


Figure 1: Comparison of serum magnesium in cases and controls

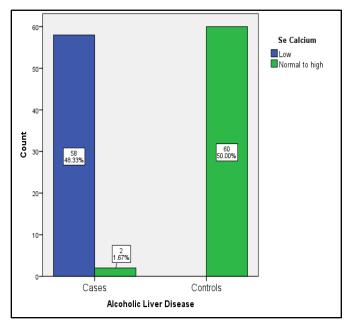
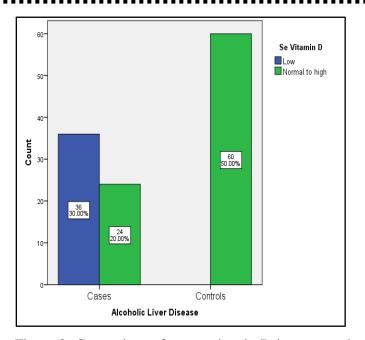
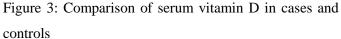


Figure 2: Comparison of serum calcium in cases and controls





The mean serum magnesium level among the cases was found to be  $1.67 \pm 0.29$  mg/dl and  $2.1 \pm 0.33$  mg/dl in controls. This reduction in mean serum magnesium level among the cases in comparison to the controls was statistically significant with a t statistic of -7.59 and p value of <0.001. (Table 1)

The mean level of serum calcium among the cases was  $7.39 \pm 0.66$  mg/dl and  $9.3 \pm 0.36$  mg/dl in controls. The mean serum calcium level was significantly lower among the cases in comparison to the control with t statistic of -19.89 and p value of <0.001. (Table 1)

The mean level of serum Vitamin D among the cases was  $9.34 \pm 7.91$  ng/ml, whereas for controls it was  $26.37 \pm 6.9$  ng/ml. The mean level of serum vitamin D was found to be significantly lowered in cases in comparison to controls with t statistic of -12.56 and p value of <0.001. (Table 1)

#### Discussion

Liver serves many important biological functions to sustain life, so early diagnosis of liver involvement is of utmost priority to prevent life threatening complications.

A study done by L Turecky et al among patients with alcoholic fatty liver disease showed that serum magnesium levels were significantly decreased in patients with alcoholic fatty liver with a mean level of  $1.63 \pm 0.24 \text{ mg/dl.}^{[5]}$  The findings of this study are concurrent to the findings obtained in our study. Similarly, a study conducted by Vatsalya V. et al. among patients with alcohol dependence showed that there was a significant drop in serum magnesium levels in patients with liver injury induced by alcohol.<sup>[8]</sup>Primary malnutrition is also a result of chronic alcohol misuse due to low dietary magnesium intake. Chronic ethanol consumption also damages the liver and pancreas and causes functional and structural problems in the gastrointestinal tract, which contribute to secondary malnutrition. Moreover, it influences the plasma membrane's magnesium transport systems either directly (via acetaldehyde-protein interactions or alcohol-related change of the phospholipid environment) or indirectly (via the decrease in cellular ATP content). Increased urine magnesium excretion as a result of ethanol-induced injury to the renal proximal tubules and the loop of Henle is one of the main causes of ethanol-induced hypomagnesaemia in alcohol abusers.<sup>[9,10]</sup>

Alcohol is a known independent risk factor for hypocalcemia resulting in osteoporosis in patients with alcoholic liver disease. A study reported by Gill GK et al. among patients with chronic alcohol intake showed that there was a significant reduction in serum calcium levels in these patients with mean serum calcium levels of  $8.11 \pm 0.93$  mg/dl which was similar to the current study finding.<sup>[11]</sup>Similarly, study conducted by Jaleel M et al. among patients with chronic liver disease showed that serum calcium levels were significantly low with increased predisposition for osteoporosis.<sup>[12]</sup>A decrease

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in the tubular reabsorption of calcium may be the result of ethanol's influence on the Na<sup>+</sup>-K<sup>+</sup>ATPase function of the proximal tubular cells.<sup>[13]</sup> The reduced tubular reabsorption of calcium may also be impacted by hypomagnesemia or suppression of parathyroid secretion by acute alcohol consumption.<sup>[14,15]</sup>

A study done by Savic Z et al. among male patients with alcoholic liver disease showed that the mean vitamin D levels were 17.95 ng/ml with 66.6% of the patients having vitamin D deficiency.<sup>[16]</sup>Similarly, a study done by Malham M et al. among patients with liver disease showed that 85% of the patients with alcoholic cirrhosis had low vitamin D levels. These findings are similar to that obtained from our study.<sup>[17]</sup>Impaired hydroxylation of vitamin D in liver, decreased production of vitamin D binding protein and an impaired cutaneous production of vitamin d owing to jaundice could be some of the reasons for the fall in vitamin d levels in such patients.<sup>[18,19]</sup>

#### Conclusion

Low serum magnesium levels as found in the current study as well as similar studies may indicate onset of liver injury in patients with alcoholic liver disease. Calcium supplementation should also be considered in patients being treated for alcoholic liver disease after estimation of serum calcium levels to prevent osteoporosis in these patients. Our study implies that vitamin D deficiency is highly prevalent in patients with alcoholic liver disease which is a strong risk factor for osteoporosis and pathological fractures in these patients. Addressing these deficiencies while treating patients with alcoholic liver disease is essential. Further research is needed to study implications of serum calcium, magnesium and vitamin D levels as diagnostic and prognostic indicators in patients with alcoholic liver disease.

#### Limitations of the study

This study does not assess the nutritional status and dietary intake of calcium, magnesium and vitamin D among the study participants. The study also did not assess the severity of liver dysfunction as well as did not quantify the amount of alcohol intake to correlate with levels of calcium, magnesium and vitamin D.

## **Ethics Committee and Consent**

Institutional Ethical Committee (IEC) approval was obtained prior the start of the study. Written consent was taken from the taken from the study participants prior to their inclusion as cases or controls.

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