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Serum Zinc Deficiency among Patients having Viral Cirrhosis

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[1,2,4]Substantial contributions to the conception or design of the work; or the acquisition, [3,5]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [6]Drafting the work or revising it critically for important intellectual content

Funding Source: None
Conflict of Interest: None

Received: July 28, 2025
Revised: Sept 02, 2025
Accepted: Oct 1, 2025

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ABSTRACT

Objective: To determine the frequency of serum zinc deficiency in patients with viral cirrhosis.

Methodology: Present descriptive cross-sectional study was done at Department of Gastroenterology Isra University Hospital, from January 2020 to July 2020. Patients aged 18 to 60 years, both genders who were presented with viral cirrhosis (Hepatitis B and C) were enrolled. Around 3 to 5 mL of venous blood was collected aseptically from cirrhotic patients for the measurement of serum zinc levels. Blood collection was centrifuged at 3,000 rpm for 10 minutes. Plasma sample analysis for zinc determination was performed on an automated Perkin-Elmer Analyst 300 atomic absorption spectrophotometer in biochemistry department to assess the zinc deficiency. All the collected data were entered into the proforma attached at the end and used electronically for research purpose.

Results: Mean of age of the patients was 49.3±13.4 years. Out of 162 patients, 88 (54.3%) were male while 74 (45.7%) were female. Diabetes mellitus was documented in 61 (37.7%) patients. Serum zinc deficiency was found in 103 (63.6%) patients. Additionally, the zinc deficiency was statistically insignificant according to age and gender of the patients (p=>0.05), while it was significantly higher among diabetes and hypertensive patients (p=<0.05).

Conclusion: Serum zinc deficiency was observed highly prevalent among viral cirrhosis patients, affecting nearly two-thirds of the study population.

Keywords: Zinc Deficiency, Liver Cirrhosis, Hepatitis B, Hepatitis C.

Cite this article as: Mohammad W, Kumar P, Munir A, Maheshwari SD, Bhutto M, Soomro M. Serum Zinc Deficiency among Patients having Viral Cirrhosis. Ann Pak Inst Med Sci. 2025; 21(4):660-664. doi. 10.48036/apims.v21i4.1341.

Introduction

Cirrhosis of liver represents the late phase of long-standing hepatic disease, marked by sever fibrosis and distortion of the hepatic normal structure due to the formation of regenerative nodules.[1] Such irreversible disorder poses a significant worldwide public health challenge, with mortality continuing to rise over recent years.[1] In the US, chronic liver disease (CLD) and cirrhosis account for a rate of mortality of around 10 deaths per 100,000 individuals.

The chronic viral hepatitis, specifically due to hepatitis B and C virus, remains a leading global cause of the liver cirrhosis and its related complications, significantly contributing to hepatic decompensation, hepatocellular carcinoma (HCC), and related mortality. The cirrhosis caused by the viral infection continues to stay a big health burden in both developed and developing nations despite improves in antiviral therapies and supportive care of the patients. In the Pakistan, the prolonged infection with hepatitis C and hepatitis B viruses is the leading cause of the liver cirrhosis, with approximately 84% of affected individuals progressing to CLD.[3]

Additionally, individuals with liver cirrhosis also frequently complicated by malnutrition and essential micronutrients deficiencies, which are related to poorer clinical outcomes and higher rate of the mortality.[4] The imbalance in micronutrient, particularly of trace elements, has emerged as an important but frequently underrecognized characteristic of CLD pathophysiology.

The Zinc is an important micronutrient that plays multiple biological roles, predominantly involving its function as the cofactor for various enzymes, the contribution of it in maintaining the proteins' structural stability, and involvement in the gene transcription and expression

control,[5] the antioxidative defense and immune function. Though, in CLD, the impaired hepatic synthesis of albumin, intestinal absorption disorder, raised excretion of zinc by urine, and portosystemic shunting leading to hypozincemia development. Subsequently the decreased albumin level among patients with cirrhosis results in decreased binding capacity of zinc, facilitating elevated urinary loss and lower circulating levels of the zinc, which further worsen as advanced severity of disease. According to Japanese cohorts of CLD patients, a higher prevalence of zinc deficiency was noted, with nearly 91% of cirrhotic patients having serum zinc concentrations below 80 µg/dL; the degree of zinc deficiency was significantly linked to the hypoalbuminemia and disease progression, highlighting the close relationship between advanced lived disease and status of zinc.[6,7]Furthermore, the other observational clinical studies have documented the frequent incidence of zinc deficiency among patients with viral cirrhosis and a possible association with the development of hepatic encephalopathy and advanced stages of disease.[8] As according to another study conducted at a tertiary care center, the level serum zinc levels were significantly lower among with viral cirrhosis compared to healthy controls, with a clear inverse correlation between Child-Pugh score and zinc level.[9]

Overall the most existing data include mixed etiological pattern of cirrhosis, and there is limited etiological specific evidence focusing exclusively on cirrhosis by viral infection, specifically in regions with a high burden of HBV and HCV. However, the present study is significant because it addresses an important knowledge gap by estimating the prevalence and clinical relevance of serum decreased zinc level specially among individuals with viral cirrhosis. Establishment of the baseline zinc status and its relation disease severity may help identify zinc deficiency as a potentially modifiable factor, support routine assessments of zinc levels in clinical practice, and provide a foundation for future interventional studies aimed to enhancing outcomes in this population.

Methodology

This descriptive Cross-Sectional Study was carried out at Department of Gastroenterology Isra University Hospital. Study was conducted during a period of six months after the approval of synopsis from January 2020 to July 2020. All the patients with age range of 18 to 60 years, both male and female patients who were infected with hepatitis B and hepatitis C and diagnosed as cirrhotic patients on the basis of CT findings (irregularly outlined shrunken liver, dilated portal vein diameter and. splenomegaly) who visited to outpatient department of Gastroenterology Isra University Hospital were included, while all the patients who were known cases of any autoimmune disease or immunodeficiency disorder, those already receiving cancer chemotherapy, patients with liver cirrhosis due to causes other than hepatitis B or C viruses, and patients with acute or chronic diarrhea were excluded. Ethical approval was obtained from CPSP Ref no CPSP/REU/GAS-2018-165-916. University Sample size of 162 cases was calculated on W.H.O sample size calculator with 95% confidence level, 7% margin of error and taking expected prevalence of serum zinc deficiency i.e. 28.9%,[9] in viral cirrhotic patients. Before to take a part of study, all the cases provided informed consent after thoroughly explanation of the study objectives, procedure, related risks, and expected benefits. The blood sample from each case for fasting plasma zinc analysis was collected. To best accuracy and contamination prevention, all the materials of the laboratory utilized for the collections of samples. The sodium heparin vacutainer tubes (BD), powder-free silicone gloves, and pipette tips were utilized, whereas all collection tubes were strictly washed with deionized water and nitric acid, subsequently drying in an oven at the 60°C. Blood collection was centrifuged at 3,000 rpm for 10 minutes. Plasma sample analysis for zinc determination was performed on an automated Perkin-Elmer Analyst 300 atomic absorption spectrophotometer in biochemistry department to assess the outcome variable i.e. zinc deficiency. The normal serum zinc level considered 11-19 mmol/L and the value <11 mmol/L was considered as low. The procedures were managed personally by the researcher under the supervision of a consultant with minimum clinical experience of five years. All the relevant data were carefully recorded using self-made study proforma.

Subsequently the Probable biases and confounding factors were concentrated by carefully following to the predefined sample selection criteria. The collected information was entered and analyzed into SPSS version 21.0. The quantitative variable like age and serum zinc level were presented by calculating mean and standard deviation. The qualitative variables like gender, socioeconomic status, diabetes mellitus, hypertension and serum zinc deficiency were presented as frequency and percentages. Effect modifiers were controlled through stratification of age groups, gender, socioeconomic status, diabetes mellitus and hypertension to see the impact of these on zinc deficiency. Chi square test as appropriate was applied and $P \leq 0.05$ was taken as significant.

Results

Based on the demographic and clinical analysis the mean age of study population was 49.3 ± 13.4 years and mean serum zinc level was 15.5 ± 5.6 mmol/L. however males comprised 54.3% of the cases, and females accounted for 45.7%. The diabetes mellitus was found in 37.7% of patients, while 45.7% of the patients were observed as hypertensive. According to the socioeconomic status, 34% of patients belonged to the lower socioeconomic group, followed by 43.8% had middle group, and 22.2% had showed upper socioeconomic status. Table I

Table I: Demographic and clinical analysis of the patients. (n=162)

Variables		Statistics
Mean age		49.3+13.4 years
Mean serum zinc level		15.5+5.6 (mmol/L)
Gender	Male	88(54.3%)
	Female	74(45.7%)
Diabetes mellitus	Yes	61(37.7%)
	No	101(62.3%)
Hypertension	Yes	74(45.7%)
	No	88(54.3%)
Socioeconomic status	Lower	55(34%)
	Middle	71(43.8%)
	Upper	36(22.2%)

The serum zinc deficiency was detected in a considerable proportion of the study population, influencing 103 (63.6%) of the patients, indicating that around two-thirds of the participants had inadequate levels of the zinc, as shown in figure 1.

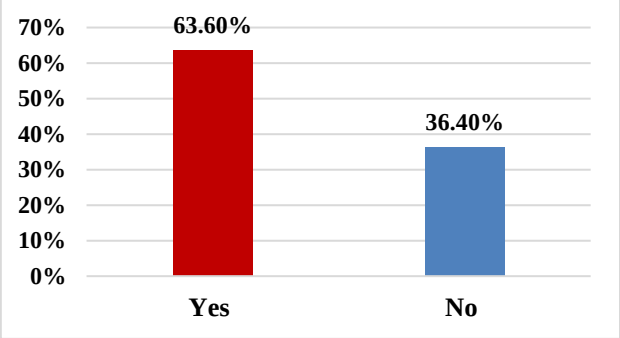

Figure 1. Frequency of Serum Zinc Deficiency. (n=162)

The stratification analysis of this study highlighted serum zinc deficiency was some more common among over 40 years aged patients (56.8%) (p = 0.394). Additionally, male patients had higher proportion of zinc deficiency (36.4%) compared to females (27.2%), p = 0.318. it was also statistically insignificant according to socio-economic status p = 0.063. However, there was a statistically significant association was of serum zinc deficiency with diabetes mellitus and hypertension p = <0.05 as shown in table II.

Table II: Stratification of age group with serum zinc deficiency. (n = 162)

Variables	SERUM ZINC DEFICIENCY		P-value
	YES	NO	
Age groups			
18 – 40	11(6.8%)	9(5.6%)	0.394
> 40	92(56.8%)	50(30.9%)	
Gender			
Male	59(36.4%)	29(17.9%)	0.318
Female	44(27.2%)	30(18.5%)	
Socioeconomic status			
Lower Class	39(24.1%)	16(9.9%)	0.063
Middle Class	26(16.0%)	10(6.2%)	
Upper Class	38(23.5%)	33(20.4%)	
Diabetes mellitus			
Diabetic	45(27.8%)	16(9.9%)	0.036
Non-Diabetic	58(35.8%)	43(26.5%)	
Hypertension			
Hypertensive	59(36.4%)	15(9.3%)	0.0001
Non-Hypertensive	44(27.2%)	44(27.2%)	

Discussion

The hepatic disorders impact millions of individuals globally on a daily basis, and cirrhosis develops as an end result of prolonged hepatic disease.[10] Among individuals with viral advanced cirrhosis, tend to have reduced serum zinc levels, which may contribute to disease progression and have been related to life-threatening clinical complications.[11] However this study was conducted among patients with viral cirrhosis to assess serum zinc deficiency, and we found that serum zinc deficiency was present in a substantial proportion of the population, affecting around 103 (63.6%) of the cases. The findings were parallel with a growing body of evidence presentation where zinc deficiency is most common in patients with cirrhosis patients and is linked to the severity of disease severity and complications, like Kakumanu V et al[1] reported that the zinc deficiency was highly prevalent among 97.6% of the cases, with mean serum zinc levels demonstrating a significant stepwise decline from Child–Pugh Class A to Class C, (50.4 µg/dL, 42.32 µg/dL and 37.02 µg/dL) respectively. Likewise, the Li X et al[12] reported that the most of the cirrhotic cases had zinc deficiency (84.5%), following by those with subclinical zinc deficiency 14.1%, and only 1.4% of the patients had normal levels of serum zinc.

In the study by Lakananurak N et al[13] reported that the serum Zinc deficiency was observed among 60% of cases and was significantly linked to the development and severity of ascites. Consistently the study from North India

by et al[8] demonstrated significantly lower zinc level among patients 40.5 ± 10.0 µg/dL compared with controls 104.0 ± 9.1 µg/dL, (p=<0.05). Likewise, the serum zinc concentrations declined significantly with increasing severity of hepatic encephalopathy and higher Child Pugh class and the MELD scores (p=<0.05).[8] Furthermore, in line with our findings, Soomro et al[14] conducted study at a tertiary care Hospital in Pakistan, where they reported that the patients with liver cirrhosis had a high frequency of zinc deficiency around 69%. The relationship between zinc deficiency and complications for instance hepatic encephalopathy is biologically reasonable. The Zinc is the cofactor for enzymes involved in the detoxification of ammonia, metabolism of the protein, and its reduction can disorder handling of the nitrogen, potentially worsening hyperammonemia and the neurocognitive dysfunctions.[8]

Comparable results have been documented by Sattar A et al[3], as the zinc deficiency was observed in 61.8% of the cirrhotic patients. Furthermore, many other studies from different populations have reported an even higher prevalence of zinc deficiency among patients with cirrhosis of liver.[10,15-18] The variations in estimated frequencies across the studies may be attributed to the differences in sample size of studies, etiological pattern of cirrhosis, nutritional status of the patients, methodological assay, and the sample selection criteria. Furthermore, the zinc deficiency appears to be directly linked to the severity of liver fibrosis, and the use of different cutoff values to define deficiency in various studies can considerably influence the reported prevalence rates of zinc deficiency.

Demographically in this study the mean age of the patients was 49.3 ± 13.4 years, and of the 162 patients, 88 (54.3%) were males and 74 (45.7%) were females. The equivalent gender distributions have been specified in previous studies including Liang CC et al[19] found 53.5% males and 46.5% females, and Mohammad S et al[20] reported 49.3% males and 50.7% females in their studies. Furthermore, based on stratification analysis of this study highlighted serum zinc deficiency was some more common among patients over 40 years of age, and a statistically significant association was observed between serum zinc deficiency and both hypertension and diabetes mellitus (p = <0.05). In aligns to our findings, it has been reported that the low serum zinc levels have been linked to advanced hepatic fibrosis in patients with type 2 diabetes and NAFLD, highlighting the role of zinc deficiency in metabolic disturbances and the potential advantages of zinc supplementation in patients with CLD.[20,21] Pakistan bears one of the highest burdens of viral hepatitis globally.[21] A substantial proportion of affected individuals progress to chronic liver disease, largely because hepatitis often remains asymptomatic and undiagnosed in most patients due to the absence of a comprehensive national screening program.[22] Despite the heterogeneity, the cumulative evidence supports a higher incidence of serum zinc deficiency in among cirrhotic patients and emphasizes its involvement with the progression of disease and complications. Such findings support the clinical importance of micronutrient assessment in CLD and propose that routine zinc estimation should be studied, remarkably in patients with advanced cirrhosis or its associated complications. Upcoming prospective and interventional studies are suggested to additional clarify whether zinc supplementation can improve clinical outcomes and lessen the disease progression in this high-risk population of CLD.

Conclusion

It is to be concluded that serum zinc deficiency was highly prevalent among viral cirrhosis patients, affecting nearly two-thirds of the study population. Additionally, the higher rate of zinc deficiency in advanced liver disease, diabetes mellitus and hypertension, suggesting that metabolic comorbidities and disease severity may exacerbate micronutrient reduction. However, the early screening and targeted correction of it may offer a practical strategy to improve metabolic status, decrease complications, and potentially enhance clinical outcomes in these vulnerable individuals. Moreover, our findings highlighted the requirement for future research to explore those factors that could be considered as higher risk of serum zinc deficiency.

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