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Serum Zinc Deficiency in Patients with Spontaneous Bacterial Peritonitis

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Author`s Contribution

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

Funding Source: None
Conflict of Interest: None

Received: June 08, 2024
Accepted: Nov 19, 2024

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ABSTRACT

Objective: To determine the frequency of serum zinc deficiency in patients with spontaneous bacterial peritonitis (SBP).

Methodology: A descriptive cross sectional study was done at Department of Medicine, Liaquat University Hospital Hyderabad from Sept 2021 to Feb 2022. Patients with spontaneous bacterial peritonitis (SBP) of at least 2 weeks' duration, aged 20–60 years, and of either gender were included in the study, and zinc deficiency (below 70 µg/dL) was further evaluated by collecting blood samples from each participant after obtaining informed consent. Data entry and analysis was done using SPSS version 26.

Results: A total of 137 SBP patients were studied with mean age of 55.64 ± 8.83 years and average duration of SBP was 6.85 ± 4.64 weeks. The study population comprised 55.5% males and 44.5% females. Zinc deficiency was observed in 86 (62.7%) patients. Furthermore the statistical significance was observed for zinc deficiency in accordance with residence (p=0.01), socio-economic status (p=0.03), smoking, (p<0.01) and obesity (p<0.01).

Conclusion: Zinc deficiency was highly prevalent, affecting 62.7% of patients with SBP, with increased prevalence among those with a history of smoking, diabetes, and obesity. Conclusively the zinc deficiency is not only a common complication in patients with cirrhosis but also plays an important role in the development and progression of spontaneous bacterial peritonitis.

Keywords: Liver cirrhosis, SBP, Zinc level.

Cite this article as: Subhan A, Neelam, lakho MA, Fareed GH, Memon N, Luhano MK. Correlation Serum Zinc Deficiency in Patients with Spontaneous Bacterial Peritonitis. Ann Pak Inst Med Sci. 2025; 20(4):769-773. doi. 10.48036/apims.v20i4.1234.

Introduction

Liver cirrhosis is characterized by widespread fibrosis and the formation of nodules, which disrupt normal liver architecture.1 This condition is associated with a reduction in hepatocellular mass, activation of hepatic stellate cells, and increased production of collagen and other extracellular matrix components, ultimately leading to fibrotic changes.[2] Most patients remain asymptomatic until the advanced stage, known as decompensated cirrhosis, which is marked by complications such as ascites, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, and variceal bleeding due to portal hypertension.[3]

The clinical assessment of patients with cirrhosis may reveal a range of findings that necessitate a hepatic or gastrointestinal-focused evaluation to identify the underlying cause.[4] Ascites is a key feature of liver cirrhosis, resulting from a combination of portal hypertension and worsening vascular dysfunction. Its presence is associated with a poor prognosis, with a high mortality rate within three years. The development of ascites increases the risk of complications such as renal impairment, SBP, and hyponatremia.[5,6]

SBP is a severe complication in cirrhotic patients with ascites. The ascitic fluid is typically transudative and has low opsonic activity, creating an environment conducive to bacterial growth. SBP prevalence ranges from 1.5–3.5% in outpatients to 10–30% in hospitalized patients.[7,8] Historically, in-hospital mortality from SBP was over 90%; however, with advances in early diagnosis and timely antibiotic treatment, this rate has decreased to approximately 20%.7 The condition is predominantly caused by gram-negative aerobic bacteria, with Escherichia coli (E. coli) being the most common pathogen, typically originating from the gastrointestinal tract. Another frequently identified organism is Klebsiella pneumoniae. The remaining cases are primarily attributed to gram-positive aerobic bacteria, most commonly Streptococcus pneumoniae or Viridans group streptococci.

Trace element and vitamin deficiencies are frequently observed in cirrhosis, regardless of its underlying cause. Compared to the general population, patients with liver cirrhosis have reduced vitamin reserves, often due to impaired liver function, inadequate dietary intake, poor absorption, and increased metabolic breakdown.[8] Among trace elements, deficiencies in calcium, magnesium, zinc, and iron are commonly detected in the serum of cirrhotic patients. Zinc deficiency, in particular, is prevalent in chronic liver conditions, including chronic hepatitis, metabolic associated with FLD, and the cirrhosis of liver.[8] As SBP is recognized as a significant predictor of mortality among patients suffering from liver cirrhosis accompanied by ascites.[5] Additionally, certain studies have suggested a potential association between zinc deficiency and an elevated risk of SBP development, emphasizing the importance of addressing trace element imbalances in these patients.[1,5,9] Zinc is a vital trace element with numerous functions in the human body. It serves as a cofactor for various enzymes and proteins that contribute to anti-inflammatory, antioxidant, and apoptotic processes.[11] Zinc plays a crucial role in maintaining cellular integrity and supporting biological functions related to cell development, division, and growth. Notably, zinc-binding proteins constitute approximately 10% of the human proteome. The liver is instrumental in regulating systemic zinc homeostasis, underscoring its importance in overall metabolic balance.[11] As the patients who died had significantly lower mean serum zinc levels compared to those who survived.[11] However the suspected pathophysiological link between zinc deficiency and SBP in cirrhosis involves impaired immune function, reduced antioxidant defenses, and compromised intestinal barrier integrity.

The deficiency of Zinc may weaken the body's ability to combat infections, increase oxidative stress, and promote bacterial translocation, contributing to the development of SBP, while the exact mechanism remain is complex and not fully understood. The rationale for this study stems from the limited and controversial evidence regarding zinc deficiency in patients with SBP and cirrhosis, particularly at the local level. This study aimed to address this gap by generating local data on the prevalence and magnitude of zinc deficiency in patients with spontaneous bacterial peritonitis. By investigating this association within our population, the study seeks to enable early identification and management of affected patients.

Methodology

A cross-sectional descriptive study was conducted at the Department of Medicine, Liaquat University Hospital Hyderabad. The study was carried out over six months, from September 2021 to February 2022, following approval of the proposal by CPSP. The study included patients aged 20-60 years of either gender with a history of abdominal distention, diagnosed with spontaneous bacterial peritonitis (confirmed by ascitic fluid DR) for ≥2 weeks. Patients already on diuretic therapy, those with known autoimmune diseases, hematological disorders, secondary bacterial peritonitis, sepsis, tuberculosis, heart failure, nephrotic syndrome, hypothyroidism, or those who were non-cooperative, refused to give consent, or chose not to participate were excluded.

All relevant admitted patients diagnosed with spontaneous bacterial peritonitis were evaluated for serum zinc levels. The researcher provided extensive counseling to all participants before obtaining informed consent. During the counseling session, participants were educated about the study's objectives, the procedures for sample collection and analysis, and any associated costs, particularly those related to the laboratory tests for zinc status. Participants were informed of their rights, including the voluntary nature of their involvement and the freedom to withdraw from the study at any time without penalty.

After obtaining consent, a 2-cc venous blood sample was drawn from each participant using a 5-cc disposable syringe and sent to the laboratory for analysis. Zinc deficiency was defined as serum zinc levels below the standard reference range, typically <70 µg/dL. The data were collected using a pre-designed proforma, and all financial costs of the study were borne by the researcher.

The study investigated the prevalence of zinc deficiency in patients with spontaneous bacterial peritonitis, considering potential effect modifiers such as obesity, smoking, diabetes mellitus, hypertension, chronic viral hepatitis B, chronic viral hepatitis C, educational status, height, weight, BMI, and socioeconomic status. Data were analyzed using SPSS version 22.0, and post-stratification chi-square tests were applied to categorical variables with a 95% confidence interval. A p-value of ≤0.05 was considered statistically significant.

Results

Based on the demographic and clinical data, the study population comprised 55.5% males and 44.5% females,

with a majority (59.1%) residing in urban areas. Smoking was reported by 40.1% of participants, while 62.0% were classified as obese. Diabetes mellitus affected 58.4% of individuals and 57.7% were observed as hypertensive. Chronic viral hepatitis B was reported in 52.6%, and hepatitis C was in 61.3%. Table I

Table I: The clinical and demographic parameters of the study population (n=137)

Parameters	Frequency	Percent
Gender		
Male	76	55.5
Female	61	44.5
Residence		
Urban	81	59.1
Rural	56	40.9
Smoking		
Yes	55	40.1
No	82	59.9
Obesity		
Yes	85	62.0
No	52	38.0
Diabetese mellitus		
Yes	80	58.4
No	57	41.6
Hypertension		
Yes	79	57.7
No	58	42.3
Chronic Heptitis B		
Yes	72	52.6
No	65	47.4
Chronic Heptitis C		
Yes	84	61.3
No	53	38.7

Zinc deficiency was observed in 62.7% of the study population, indicating a significant prevalence. **Figure 1.**

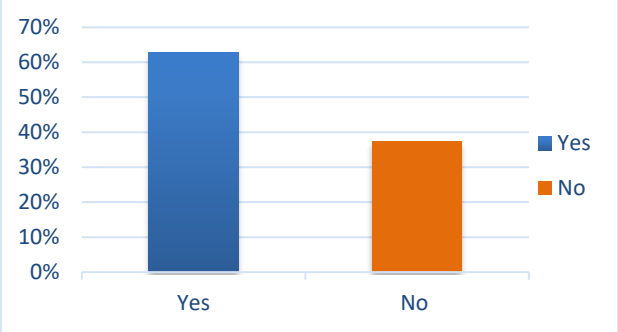

Figure 1. Frequency of zinc deficiency. (n=137)

Zinc deficiency was significantly associated with urban residence (67.4%, p = 0.016), lower socioeconomic status (36.0%, p = 0.038), smoking (51.2%, p = 0.001), obesity (70.9%, p = 0.001), and diabetes mellitus (65.1%, p = 0.034). Gender and age were not statistically significant factors. Table II

Table II: Zinc deficiency based on clinical and demographic parameters in the study population. (n=137)

Variables		ZINC DEFICIENCY		Total	p-value
		Yes	No		
AGE (years)	20-29	12(14.0%)	4(7.8%)	16(11.7%)	0.574
	30-39	21(24.4%)	17(33.3%)	38(27.7%)	
	40-49	29(33.7%)	16(31.4%)	45(32.8%)	
	50-60	24(27.9%)	14(27.5%)	38(27.7%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
Gender	Male	51(59.3%)	25(49.0%)	76(55.5%)	0.246
	Female	35(40.7%)	26(51.0%)	61(44.5%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
Residence	Urban	58(67.4%)	23(45.1%)	81(59.1%)	0.016
	Rural	28(32.6%)	28(54.9%)	56(40.9%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
SES	Lowe	31(36.0%)	30(58.8%)	61(44.5%)	0.038
	Middle	34(39.5%)	12(23.5%)	46(33.6%)	
	Upper	21(24.4%)	9(17.6%)	30(21.9%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
Smoking	Yes	44(51.2%)	11(21.6%)	55(40.1%)	0.001
	No	42(48.8%)	40(78.4%)	82(59.9%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
Obesity	Yes	61(70.9%)	24(47.1%)	85(62.0%)	0.001
	No	25(29.1%)	27(52.9%)	52(38.0%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	
Diabetes mellitus	Yes	56(65.1%)	24(47.1%)	80(58.4%)	0.034
	No	30(34.9%)	27(52.9%)	57(41.6%)	
Total		86(100.0%)	51(100.0%)	137(100.0%)	

Discussion

The formation of fibrosis and cirrhosis in the liver is a multifaceted process influenced by various factors, and it is suggested that serum zinc levels are related to cell division and growth in the liver. SBP is a common and serious complication in patients with liver cirrhosis and ascites, leading to significant morbidity and mortality if left untreated.[12,13] Zinc deficiency and altered metabolism are common in various liver diseases, including alcoholic and viral liver conditions.[14] These deficiencies can result from multiple factors, such as insufficient dietary intake, increased zinc excretion through urine, activation of specific zinc transporters, and the induction of hepatic metallothionein.[15]

Zinc is essential for the immune system, acting as a cofactor for enzymes involved in numerous cellular and metabolic processes. It also helps in regulating oxidative stress and exerts anti-inflammatory effects. With the rise in antibiotic resistance, the prevention of SBP has become a critical issue.[5] If zinc deficiency is found to be a predictor of SBP, supplementing zinc in patients with cirrhotic ascites could help decrease the risk of infections, reduce the need for unnecessary antibiotic treatments, and significantly lower the associated morbidity and mortality in this high-risk group.[17-22] This study underscores the link between low serum zinc levels and the onset of SBP in patients with cirrhotic ascites, with a 62.7% prevalence

of zinc deficiency, which is consistent with the findings of Hanna MA et al[5] who reported that 67.6% of patients with cirrhotic ascites and low serum zinc developed SBP, while 94.9% of SBP patients had low serum zinc levels.

Other studies, including those by the Abd Ellatif Afifi M et al[1], have proven that the lower serum zinc level is significantly predictive of SBP development, with a threshold level of ≤70 μg/dL showing a sensitivity of 84% and specificity of 64%. Additionally they highlights the importance of monitoring zinc levels in cirrhotic patients, particularly those with hepatitis C virus, as significantly lower serum zinc levels were observed in these individuals diagnosed with SBP.[1] Consistently, Mohammad A. et al[23] found that zinc deficiency was an independent risk factor for the development of SBP in cirrhotic patients, with a significant association ($p = 0.001$). In their multivariate analysis, low ascitic protein levels (≤1 g/dL) and low zinc status emerged as strong predictors of SBP, further supporting the role of zinc deficiency in the pathophysiology of SBP in cirrhosis. These findings suggest that serum zinc levels may serve as both a diagnostic and prognostic marker for SBP, and addressing zinc deficiency could play a crucial role in preventing infections and improving patient outcomes.[1]

Regular monitoring of serum zinc levels in patients with liver cirrhosis and ascites is very essential for early identification of deficiency. Supplementation of the Zinc should be prioritized for deficient patients, particularly those with risk factors such as low ascitic protein or a history of SBP, to reduce infection risk and enhance clinical outcomes. This study only evaluated serum zinc levels and did not consider other biomarkers or potential confounders, such as medications and liver disease severity, and lacked a control group of cirrhotic patients without SBP; therefore, further research should include multi-center, longitudinal studies with larger, more diverse populations, incorporating additional biomarkers of zinc deficiency and exploring the effects of zinc supplementation on SBP development.

Conclusion

Zinc deficiency was observed in a significant proportion of cirrhotic patients with SBP. Several factors, including poor socioeconomic status, smoking, obesity, and diabetes mellitus, were more commonly associated with zinc deficiency in these patients. In conclusion, zinc deficiency is not only a prevalent complication in patients with cirrhosis but also plays a crucial role in the development and progression of spontaneous bacterial peritonitis. Therefore, zinc deficiency should be considered an important risk factor when managing SBP in cirrhotic patients.

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