



## RESEARCH ARTICLE

### STUDY ON PREVALENCE OF HYPONATREMIA IN HEPATIC CIRRHOSIS AND ITS CORRELATION WITH COMPLICATIONS AND SEVERITY OF CIRRHOSIS

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#### ABSTRACT

**Aims and Objective:** Hyponatremia is the most common electrolyte disorder seen in advanced cirrhosis. The aim of the present study is to study the prevalence of hyponatremia in cirrhosis and evaluate the association between serum sodium level and complications with severity of cirrhosis.

**Materials and Method:** Study was an observational study conducted at RIMS, Ranchi from October 2014 to October 2015. The patients were evaluated with detailed history, physical examination and relevant investigations.

**Results:** The mean age of the patients was  $44.89 \pm 10.27$  years there was a significant association between hyponatremia and hepatic encephalopathy, hepatorenal syndrome and portal hypertension. There was also a significant association between degree of hyponatremia and severity of cirrhosis as judged by modified Child-Pugh score and MELD score.

**Conclusion:** Hyponatremia is a common finding in cirrhotic patients. Thus early treatment and early detection can prevent complications and improve the quality of life.

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## INTRODUCTION

Hyponatremia is a common finding in patients with decompensated cirrhosis due to an abnormal regulation of body fluid homeostasis. (Epstein, 1985; Gines *et al.*, 2006) Although hyponatremia in cirrhosis was described more than 50 years ago, (Eisenmenger *et al.*, 1950) its importance in the clinical assessment of patients with cirrhosis was overlooked for many years. Hyponatremia is defined as serum sodium less than 135 meq/L. It is the most common electrolyte disorder. Its homeostasis is vital to the normal physiologic function of cells. A disturbance in body water homeostasis is a common feature of advanced cirrhosis. (Gines *et al.*, 1994; Hecker and Sherlock, 1956; Shear *et al.*, 1965) According to several recent studies, hyponatremia occurring as a result of a reduced solute free water clearance was a key prognostic factor in patients with liver cirrhosis when hyponatremia was incorporated into the MELD score. (Arroyo *et al.*, 1976; Angeli *et al.*, 2006) Little is known regarding degree of dilutional hyponatremia and development of cirrhotic complications. The aim of this study was to study the prevalence of hyponatremia in cirrhosis and evaluate the association between serum sodium level and complications and severity of cirrhosis.

## MATERIAL AND METHODS

This observational study was conducted on 100 patients admitted in various wards of Department of Medicine, Rajendra institute of medical science, Ranchi between October 2014 to October 2015 with cirrhosis of liver. Informed consent was obtained from all patients enrolled for the study. The data of the patients was obtained in a well designed performa. All relevant investigations were done in Departments of Biochemistry, Pathology, Surgery and Radiology of Rajendra Institute of Medical Sciences, Ranchi. After admission, a detailed history was obtained, and a thorough physical examination was performed. Blood samples were obtained to measure serum osmolality and serum levels of sodium, PT, INR, urea and creatinine and to perform standard liver function test. All patients underwent an USG whole abdomen and upper GI endoscopy. The diagnosis of liver cirrhosis was based on characteristic findings, including physical stigmata of cirrhosis, decreased serum albumin, ultrasonography findings of a nodular liver surface, coarsened echogenicity of liver parenchyma, an enlarged spleen and / or ascites and the detection of esophageal varices by endoscopy.

### Inclusion Criteria

All patients with cirrhosis of liver diagnosed on the basis of USG whole abdomen, clinical examination and on the presence

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of signs and symptoms of chronic liver disease in compensated or decompensated state.

### Exclusion Criteria

Patients with cardiac failure, patients with CKD, patients on diuretic therapy, patients on drugs like Selective serotonin reuptake inhibitors (SSRI), Monoamine oxidase (MAO) inhibitors, Tricyclic antidepressants (TCA) etc. Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data are made. Assumptions: 1. Dependent variables should be normally distributed 2. Samples drawn from the population should be random, and cases of the samples should be independent. Chi square / Fisher exact Test have been used to find the significance of study parameters on categorical scale between two or more groups.

## RESULTS

**Table 1. Demography Details**

Parameters	n=100
Age(years) (Mean ±SD)	44.89±10.27
Sex	Number (%)
Male	84(84%)
Female	16(16%)
Cause of Cirrhosis	Number (%)
Alcohol	96(96%)
HBV	4(4%)
HCV	0
Other	0
MELD SCORE (Mean+ SD)	22.77±8.26
Serum sodium (meq/L) (Mean+ SD)	127.9±11.29
≤130 meq/L	34(34%)
131-135 meq/L	20(20%)
≥136 meq/L	46(46%)

The mean age of the patients was 44.89 ±10.27 years (range, 22-70 years) and consisted of 84 (84%) men and 16 (16%) women. Causative factors for liver cirrhosis included alcoholic liver disease (96 cases, 96%), chronic hepatitis B (4 cases 4%). The mean MELD score was 22.77 ±8.26 and mean serum sodium concentration was 127.9±11.29 meq/L.

**Table 2. Characteristics of Patients according to Serum Sodium Concentration serum sodium**

Patient's characteristics	≤130 meq/L N=34	131-135 meq/L N=20	≥136meq/L N=46	P value
Age (years) (Mean±SD)	45.47±10.28	45.75±11.93	44.09±9.64	0.77 (NS)
Sex N(%)				
Male	29(85%)	17(85%)	38(83%)	0.94(NS)
Female	5(15%)	3(15%)	8(17%)	
Cause of Cirrhosis N (%)				
Alcohol	32(94%)	20(100%)	44(96%)	0.055(S)
HBV	2(6%)	0(0)	2(4%)	
HCV	0(0)	0(0)	0(0)	
Others	0(0)	0(0)	0(0)	
MELD Score Mean±SD	25.9±8.09	28.0±8.38	18.17±5.59	<0.0001(HS)
Child Pugh Score	10.5±1.6	9.8±1.7	7.8±1.6	<0.0001(HS)
Child Pugh class				
Class A	1	1	15	0.0002(S)
Class B	13	9	23	
Class C	20	10	8	

NS- statistically non significant, S-Statistically significant, HS- statistically highly significant

Based on the diagnostic criteria for hyponatremia in patients, out of the 100 patients of liver cirrhosis 34(34%) patients had concurrent severe hyponatremia with serum sodium concentrations ≤130 meq/L while 20(20%) patients had mild hyponatremia with serum sodium concentrations between 131-135 meq/L. However, 46(46%) patients had their serum sodium levels more than equal to the 136 meq/L. To assess the association between serum sodium and patient's characteristics, patients were classified into three groups (≤130 meq/L, 131-135 meq/L and ≥136meq/L) according to level of serum sodium. No statistical difference was found in the age groups, there was no significant difference on the basis of gender. The causative factor among these three groups were also comparable and no statistical difference was found in this respect. Serum sodium values were strongly associated with the severity of cirrhosis as assessed by Child Pugh class and MELD score. A low serum sodium had significantly high Child-Pugh class compared to normal serum sodium. All patients presented to the hospital with abdominal distension. Only one patient with liver cirrhosis was having concurrent seizures at the time of hospital admission. There was significant difference in three groups with respect to complications in liver cirrhosis namely portal hypertension, hepatic encephalopathy, hepatorenal syndrome. However no statistical significance was found in three groups with respect to ascites, GI bleeding and coagulopathy.

**Table 3. Clinical Presentation of patients at the time of admission**

Presentation	Number of patients	%
Abdominal distension	100	100%
Lower limb swelling	99	99%
Jaundice	100	100%
Altered sensorium	50	50%
Gastrointestinal bleeding	24	24%
Seizures	1	1%

## DISCUSSION

Hyponatremia is an electrolyte imbalance that commonly occurs in patients of cirrhosis of liver. Most cases are dilutional hyponatremia caused by the impairment of solute free water clearance. Studies has shown that severity of hyponatremia are associated with high complications of cirrhosis. (Adroque and Madias, 2000) In recent years, hyponatremia has attracted interest as a possible prognostic factor for liver cirrhosis.

**Table 4. Frequency of complications by serum sodium concentration**

Complications	≤130 meq/L N=34	131-135 meq/L N=20	≥ 136 meq/L	P value
Ascites	34(100%)	19(95%)	45(97.8%)	0.062
Portal hypertension	34(100%)	19(95%)	37(80.4%)	0.01
Hepatic encephalopathy	20(59%)	10(50%)	4(8.7%)	< 0.0001
GI bleeding	11(32.4%)	4(20%)	9(19.6%)	0.69
Coagulopathy	4(11.8%)	2(10%)	3(6.5%)	0.70
Hepatorenal syndrome	6(17.6%)	3(15%)	0(0)	0.014

We conducted this observational study to examine the prevalence of hyponatremia and association between hyponatremia and occurrence of major complications in patients with liver cirrhosis and severity of cirrhosis. In the present study the results indicate that a large proportion of patients with cirrhosis have abnormal values of serum sodium concentration. In fact, more than one half (54%) of patients with cirrhosis had values of serum sodium concentration below the normal range (<135 meq/L) and one third (34%) had values < 130 meq/L. Angeli *et al.* (2006) conducted multi center study in overseas countries, 997 patients with liver cirrhosis and concurrent ascites, were assigned to three groups based on serum sodium concentration, in a manner similar to that of the current study. The prevalence of hyponatremia at a serum sodium ≤135 meq/L, <130 meq/L was 49.4%, 21.6% respectively. Jong Hoon Kim *et al* (2009) showed the prevalence of hyponatremia as 27.1%, 20.8% AND 52.1% in patients with serum sodium <130 meq/L, 131-135 meq/L and > 135meq/L respectively. In the present study serum sodium values was not associated with age, sex or etiology of cirrhosis but were strongly associated with the severity of cirrhosis as assessed via Child –Pugh class and MELD score. Low serum sodium had significantly high Child-Pugh class compared to normal serum sodium. Low serum sodium also associated with high MELD score.

### Conclusion

Dilutional hyponatremia is frequent in cirrhotic patients and low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis like hepatic encephalopathy, hepatorenal syndrome and portal hypertension and high morbidity and mortality. Thus prevention, early detection, early treatment will decrease the complications in patients with cirrhosis, improve the quality of life and will improve the prognosis and will be of great advantage.

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