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The Impact of Hyponatremia on Severity of Decompensated Chronic Liver Disease

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Abstract **Original Research Article**

Introduction: Hyponatremia in cirrhosis is low sodium concentration in the blood. It has been additionally reported that hyponatremia occurs when serum sodium concentration in the blood is less than 135mmol/L, with severe hyponatremia being below 120 mmol/L. In general, two kinds of hyponatremia may be found in patients with cirrhosis, such as hypovolemic and hypervolemic hyponatremia. Complications may arise in case of correcting hyponatremia too quickly. The study aims to investigate the impact of hyponatremia on the severity of decompensated chronic liver disease. ***Methods:*** A Prospective cross-sectional study was carried out at the Department of Gastroenterology and Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shabagh, Dhaka, from March 2014 to February 2015. A total of 100 patients (N=100) for one year were enrolled in this study following the inclusive criteria. Data were collected using the predesigned semi-structured questionnaire. Verbal consent was taken before recruiting the study population. Completed data forms were reviewed, edited, and processed for computer data entry. ***Result:*** Among hundred patients (N=100) with decompensated chronic liver disease observe the impact of hyponatremia with the severity of complications. Of them, it was observed that more than one-third of the patients (37, 37.0%) belonged to age 31-40 years. The mean age was found 42.2±SD years. It was observed that almost two-thirds of the patients (63, 63.0%) were male and thirty-seven (37,37.0%) patients were female. Among the study population, the majority of the patients (90, 90.0%) belonged to serum sodium ≤135 mmol/l (Hyponatremia). The mean serum sodium was found 124.7±SD mmol/l. The majority of patients (57,57.0%) had moderate ascites, nineteen patients (19,19.0%) had mild and about one-fourth of the patients (24,24.0%) had severe ascites**.** ***Conclusion:*** Hyponatremia was a common feature in patients with chronic liver disease and its severity increased with the severity of liver disease.

Keywords: Hyponatraemia, Serum Sodium, Ascites, Cirrhosis etc.

INTRODUCTION

Hyponatremia in cirrhosis is low sodium concentration in the blood [1]. It has been additionally reported that hyponatremia occurs when serum sodium concentration in the blood is less than 135mmol/L, with severe hyponatremia being below 120 mmol/L [2, 3]. In general, two kinds of hyponatremia may be found in patients with cirrhosis, such as hypovolemic and hypervolemic hyponatremia. The initial one is symptomatic of a low concentration of sodium and concentrated volume of plasma and the second one is symptomatic of considerable impairment of the excretion of solute- free water, which results in the irregular retention of water and this mainly occurs in patients having cirrhosis and ascites [4]. An increased threat of mortality is around 12% for every unit of decrease in the serum sodium concentration [5]. Patients with hyponatremia have a greater rate of mortality compared to those patients without hyponatremia [6]. Patients with hyponatremia have a higher risk of early

death before transplantation, and hyponatremia was found to be a risk issue for amplified morbidity and mortality after liver transplantation [7]. Based on a person's body fluid eminence the reasons behind hyponatremia are normally classified as low volume, normal volume and high volume [3]. Lowvolume hyponatremia may arise from severe diarrhoea, vomiting, diuretics and sweating. Normal volume hyponatremia is classified into cases with dilute urine and concentrated urine; in which urine is dilute include adrenal insufficiency, hypothyroidism and drinking too much beer or water and insufficient antidiuretic hormone secretion. High-volume hyponatremia can occur from heart failure and kidney failure that can lead to falsely low sodium measurements including high blood protein levels, such as high blood sugar, high blood fat levels and multiple myeloma [7, 8]. Hyponatremia is the utmost common kind of electrolyte imbalance [9]. Complications may arise in the case of correcting hyponatremia too quickly [2]. Hyponatremia was one of the major threats associated with increased morbidity and mortality after liver transplantation [6, 10]. The impaired contractile alertness to stress, diastolic dysfunction, and electrophysiological abnormalities are labelled as 'cirrhotic cardiomyopathy' in the absence of known cardiac disease [11]. Despite the upsurge in baseline cardiac output, an impaired cardiac vascular response to pharmacological or physiological stress may be present [12, 13]. Even with the use of invasive monitoring, it is problematic to measure intravascular volume in patients with cirrhosis [14]. Cautious renewal with hypertonic sodium chloride should be kept only for patients with serious acute symptomatic hyponatremia and often with adjacent monitoring to evade complications. This study intends to determine the impact of hyponatremia on the severity of the decompensated chronic liver disease.

OBJECTIVES

General Objective

To investigate the impact of hyponatremia on severity of decompensated chronic liver disease.

METHODS

A Prospective cross-sectional study was carried out Department of Gastroenterology and Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shabagh, Dhaka, from March 2014 to February 2015. A total of 100 patients (N=100) over the period of one year were enrolled in this study following the inclusive criteria. Data were collected using the predesigned semi-structured questionnaire. Consecutive sampling technique was used. Verbal consent was taken before recruiting the study population. Ethical clearance was taken from the IRB Ethical Review Committee of BSMMU, Dhaka. The information was kept confidential only to be used for the study purpose.

Inclusion Criteria

- Patients with ≥18 years old presented with decompensated cirrhosis.

Exclusion Criteria

- Patients with several chronic diseases, intrinsic renal disease, intrinsic central nervous system, congestive heart failure.
- Patients who showed unwillingness to participate in the study.

Data Analysis

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies, percentages, crosstabulations were used for descriptive analysis. χ 2 test was used to analyze statistical significance. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0 and ANOVA test. The significance level of 0.05 was considered for all tests.

RESULT

Among hundred patients (N=100) with decompensated chronic liver disease observe the impact of hyponatremia with the severity of complications. Of them, it was observed that more than one-third of the patients (37,37.0%) belonged to age 31-40 years. The mean age was found 42.2±SD years. It was observed that almost two-thirds of the patients (63,63.0%) were male and thirty-seven (37,37.0%) patients were female. The majority of patients (27,27.0%) were service holder, about one-fifth of the patients (21,21.0%) were cultivator, eighteen patients (18,18.0%) were housewives, around one-sixth of the patients (16,16.0%) were businessman and eighteen patients (18,18.0%) were others occupational status. Forty-two patients (42,42.0%) have income<5000 taka/month, twenty-eight patients (28,28.0%) earn 5000-20,000 taka/month and only twenty patients (20,20.0%) earn>20,000 taka/month. Almost half of the patients (47,47.0%) had HBV, twenty-seven (27,27.0%) had HCV, six (6,6.0%) had Wilson, five (5,5.0%) had NASH and fifteen patients (15,15.0%) had unknown etiology **[Table 1].** Among the study population, the majority of the patients (90,90.0%) belonged to serum sodium ≤135 mmol/l (Hyponatremia). The mean serum sodium was found 124.7±SD mmol/l. The majority of patients (57,57.0%) had moderate ascites, nineteen patients (19,19.0%) had mild and about one-fourth of the patients (24,24.0%) had severe ascites. Based on encephalopathy, the majority of the patients (58,58.0%) were grade 1, twenty two patients (22,22.0%) were grade 0, seventeen

patients (17,17.0%) were grade II and three patients (33.0%) were grade III **[Table 2].** It was observed that nine patients (9,9.0%) were found with hepatorenal syndrome and ninety- one patients (91,91.0%) were without hepatorenal syndrome **[Table 3].** It was observed that mild ascites were found in eleven hyponatremic patients (11,12.2%) and eight normal serum sodium patients (8,80.0%), moderate ascites were found in fifty-five (55,61.1%) hyponatremic and in two (2,20.0%) normal serum sodium patients & severe ascites was found in twentyfour hyponatremic patients (24,26.7%) and no ascites was found in normal serum sodium patient **[Table 4].** Mild ascites were found in eleven patients and their mean serum sodium was found 132.0±2.9 mmol/L, moderate ascites was found in fifty-five patients and their mean serum sodium was found 123.2±5.8 mmol/L, severe ascites were found in twenty-four patients and their mean serum sodium was found 119.7±7.3 mmol/l The mean difference was statistically significant ($p<0.05$) among three groups **[Table 5].**

Table 1: Distribution of study population based on characteristics (N=100)

Characteristics	**(N,%)**
Age **Mean age:** 42.2±SD	
≤30	11, 11.0%
31-40	37, 37.0%
41-50	36, 36.0%
51-60	14,14.0%
>60	2, 2.0%
Sex	
Male	63,63.0%
Female	37,37.0%
Occupational Status	
Service	27,27.0%
Cultivator	21,21.0%
Housewife	18,18.0%
Business	16,16.0%
Others	18,18.0%
Monthly Income	
<5000/month	42,42.0%
5000-20,000/month	38,38.0%
>20,000/month	20,20.0%
Etiology	
HBV	47,47.0%
HCV	27,27.0%
Unknown	15,15.0%
Wilson	6,6.0%
NASH	5,5.0%

Table 2: Distribution of study population based on Epidemiology (N=100)

Epidemiology	**(N,%)**
Serum sodium (mmol/L) **Mean:** 124.7±7.8	
≤135 (Hyponatraemia)	90,90.0%
>135 (Normal)	10,10.0%
Ascites	
Mild	19,19.0%
Moderate	57,57.0%
Severe	24,24.0%
Encephalopathy	
Grade 0	22,22.0%
Grade I	58,58.0%

Grade II	17,17.0%
Grade III	3,3.0%

Table 3: Distribution of study population based on Hepatorenal Syndrome (N=100)

Syndrome	**(N,%)**
Hepatorenal syndrome	
Absent	91,91.0%
Present	9,9.0%

Table 4: Distribution of study population based on Serum sodium with ascites (N=100)

Ascites	**Serum sodium**	
	Hyponatremia (n=90)	Normal (n=10)
Mild	11,12.2%	8,80.0%
Moderate	55,61.1%	2,20.0%
Severe	24,26.7%	0,0.0%

Table 5: Distribution of study population based on Mean serum sodium level in ascites with hyponatraemia (n=90)

Ascites	**Serum sodium (mmol/L)**			
	Hyponatremia (n=90)	**Mean±SD**	Range (min,max)	*p-value*
Mild	11,12.2%	132.0±**SD**	127,135	
Moderate	55,61.1%	123.2±**SD**	108,135	0.001[s]
Severe	24,26.7%	119.7±**SD**	108,134	

s=significant

p-value reached from ANOVA test.

DISCUSSION

Hyponatraemia is often found in patients with ascites inferior to radical cirrhosis and hypertension [15]. Hyponatraemia in cirrhosis has been related to increased mortality and is frequent in patients with advance stage liver disease [16, 10]. Around 997 cirrhotic patients showed an occurrence of serum sodium levels less than 130 mmol/L of21.6% in 2006 [17]. In this current analysis, more than one-third of the patients (37,37.0%) belonged to age 31-40 years. The mean age was found 42.2±SD years. A similar study found that the mean age of the patients was 44±SD years [18]. Another related article found that the mean age of the patients was 46.8± SD years, which is comparable with the current study [19]. On the other hand, the mean age was 59±SD years with the range from 39to 75 years found in another article [20]. Cirrhosis is more common in adults ages 45 to 54 and about 1 in 200 adults has cirrhosis [21].

In this current study, it was observed that almost two third (63.0%) of patients were male and 37(37.0%) patients were female which indicates that chronic liver disease is predominant in male subjects. Another study found that men were 2-fold more likely to die from chronic liver disease and cirrhosis compared to women [22]. Another related study stated that women had a lower proportion of cirrhosis deaths caused by liver diseases [23].

Regarding the aetiology of chronic liver disease, it was observed in this series that HBV and HCV were most common, which were 47.0% and 27.0% respectively. However, 15.0% had unknown aetiology, 6.0% had Wilson and 5.0% had NASH. Another related study suggested that, in chronic Hepatitis B, the threat of cirrhosis depends to a large extent on the burden of viral infection and in chronic Hepatitis C; progression to cirrhosis depends primarily on the patient's age [24]. Another study found that the Hepatitis C virus was seen in 45.9% of patients [20].

Another study suggested that cirrhosis was alcoholrelated in 50.3% of patients, Hepatitis C related in 32.4% and Hepatitis B related in 9.8% of patients. Patients in Central Europe were more likely to have alcohol abuse as an aetiology of cirrhosis whereas Hepatitis C was most common in Western Europe [25]. In another study, the author depicted that the aetiology of cirrhosis was alcoholic in 19.0%, virus related in around three-fifths of the patients, and unknown in 6.0% and in 3.0% of cases a double aetiology was recognized. No patient had primary biliary cirrhosis, Wilson's disease or haemochromatosis [26].

In this present study, it was observed that the majority (90.0%) of patients belonged to serum sodium ≤135 mmol/l (Hyponatremia). The mean serum sodium was found 124.7±7.8 mmol/L. Another study found that the mean sodium level was 135±7 mmol/L which was comparable to a recent study [20]. Another related study found that 3.5% of patients presented severe hyponatraemia with serum sodium concentration ≤127 mmol/L at the time of surgery and half of the patients developed neurological complications in the early postoperative period [16]. Another study found that, in a population survey of 997 patients with cirrhosis, 486(49.6%) and 211(21.6%) had serum sodium <135 mequ/L and <130 meq/L respectively [27].

In this current study, it was observed that the majority (57.0%) of patients were found moderate levels of ascites, 19.0% were mild and 24.0% were severe. Another study found that moderate ascites was 37.8%, severe was at 53.5% and refractory ascites at 8.7%, which differ from the current study, may be due to injudicious use of diuretics and free water intake [28].

In this series, it was observed that the majority (58.0%) of patients were in Encephalopathy grade I, 22.0% in grade 0, 17.0% in grade II and 3.0% in grade III. Another related study found that severe recurrent or refractory encephalopathy was present in 15.0%, which is comparable with the current study [29].

In this present analysis, it was observed that nine patients (9,9.0%) were found with hepatorenal syndrome and ninety-one patients (91,91.0%) were without the hepatorenal syndrome. Another study suggested that refractory ascites was a common complication of advanced cirrhosis and was associated with the hepatorenal syndrome and hepatic hydrothorax [30].

In this series, it was observed that group mild ascites was found in 11 patients and their mean serum sodium was found 132.0±2.9 mmol/L. Moderate ascites were found in 55 patients and their mean serum sodium was found 123.2±5.8 mmol/L. Severe ascites were found in 24 patients and their mean serum sodium was found 119.7±7.3 mmol/L. The mean serum sodium level significantly ($p<0.05$) declined according to the severity of ascites. Another author observed that 58 patients with low serum sodium were in Class B ($p=0.001$). A more severe grade of ascites was present in patients with low serum sodium. Grade 2 ascites were present in 12/58, grade 3 in 33/58 patients and refractory ascites in 13/58 patients with serum sodium < 135 meq/l ($p<0.05$) needing frequent paracentesis and higher dosages of diuretics [28].

Treatment of hyponatraemia in patients with cirrhosis is a challenge. Early management of patients with cirrhosis with hyponatraemia should be the assessment of volume status and detection of the causes of hyponatraemia.

CONCLUSION

Hyponatraemia is a frequent finding in advanced cirrhosis. Though it is hardly enough to describe a life-risking state, hyponatraemia may have an adverse prognostic significance as it specifies an advanced disease with severe cardiovascular dysfunction. Hyponatraemia in patients with cirrhosis, can be managed with fluid restriction.

Limitations

- The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country.
- The present study was conducted at a very short period of time.
- Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size.

RECOMMENDATIONS

There is a necessity for setting a screening docket to cover all age groups for early detection and treatment of cases. Furthermore, strategies should be implemented to accelerate government programs. Further studies should be undertaken by including large number of patients.

FUNDING

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CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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