HYPONATREMIA AND ITS CORRELATION WITH HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS LIVER

Muhammad Abdur Rahman Afridi[1], Zafar Ali[2], Riaz Muhammad[3], Muhammad Asghar[4], Muhammad Faheem Afridi[5], Abu Bakkar Alam[6], Intekhab Alam[7]

[1-7] Department of Medicine, Lady Reading Hospital, Peshawar - Pakistan.
Address for Correspondence:
Dr. Riaz Muhammad
Assistant Professor (Medicine), Medical "A" Unit, Lady Reading Hospital, Medical Teaching Institution, Peshawar - Pakistan.
Email: dr.saifriaz@gmail.com
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ABSTRACT

Objective: To determine hyponatremia and its correlation with hepatic encephalopathy in liver cirrhosis patients in a teaching hospital.

Methodology: A descriptive study was carried out from April 2013 to May 2014, in the Department of Medicine, Lady Reading Hospital, Peshawar. The study included 130 patients with liver cirrhosis. Hyponatremia was identified among these. Hepatic encephalopathy (HE) was diagnosed and graded according to the West Haven classification into four grades. For data entry and analysis, SPSS version 21.0 was utilized. Spearman rank test was used for determining the relationship of hyponatremia and severity of hepatic encephalopathy.

Results: Of the 130 patients, males were 76 (58.5%) and females were 54 (41.5%). Mean age of study patients was 55.52 ±10.144 years. Hyponatremia was present in 48 (36.9%) patients. Mild Hyponatremia was present in 12 (9.2%), Moderate in 28 (21.5%) and Severe in 8 (6.2%) patients. Hepatic encephalopathy was present in 88 (67.7%) patients. Hepatic encephalopathy grade I was present in 27 (20.8%), grade II in 31 (23.8 %), grade III in 16 (12.3 %), and grade IV in 14 (10.8%) patients. In 48 patients with hyponatremia, 42 were found to have HE (r =0.32, p value <0.001). Correlation of severity of hyponatremia with grades of HE showed (r =0.33, p value <0.001).

Conclusion: Hyponatremia was found with increased frequency in patients with cirrhosis liver. The relationship of hyponatremia with frequency and severity of hepatic encephalopathy was statistically significant.

Key Words: Hyponatremia, Cirrhosis liver, Hepatic encephalopathy

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INTRODUCTION

Cirrhosis liver is one of the leading causes of morbidity and mortality[1]. It is a very common health problem challenging the health professionals. It is on the rise in Pakistan, because of the high prevalence of hepatitis B and C[2]. Patients with cirrhosis liver frequently develop complications like hepatic encephalopathy. The patients manifest with altered conscious level, difficulty in judgment, day night reversal of sleep, flapping tremor of hands and irrelevant talking or speech[3]. Similarly, there is impairment in regulation of body fluid homeostasis in patients with cirrhosis liver. In a number of patients, the kidneys retain the water excessively as compared to sodium. This may results in significant derangement of sodium concentration in the serum, which is termed as hyponatremia[4]. Hyponatremia is considered to be a marker of worsening of the disease and increases the risk of hepatic encephalopathy about eight folds[5]. It might lead to deterioration in terms of grades of hepatic encephalopathy as well[6]. The cut-off limit for serum sodium in healthy subjects is 135meq/L. However, in cirrhotic patients, hyponatremia is labeled when the concentration of serum sodium is <130 meq/l). By this definition, the reported prevalence of hyponatremia in cirrhotic patients is 20%[7]. In another study by Qureshi et al, 30.7% of patients had serum sodium <130 meq/l[8].

The purpose of this study was to determine the frequency of hyponatremia in patients with cirrhosis liver and to correlate it with the frequency and severity of HE. If found to be significantly high among patients with HE due to liver cirrhosis, routine screening for Hyponatremia will be suggested in patients with HE and those with liver cirrhosis without HE. This will help us in developing recommendations for reconsideration of current guidelines regarding management of patients with HE and Hyponatremia and thus help in reducing the morbidity and mortality associated with HE with Hyponatremia.

METHODOLOGY

A descriptive study was carried out from April 2013 to May 2014, in the Department of Medicine, Lady Reading Hospital, Peshawar. The study included 130 patients with liver cirrhosis. Hyponatremia was identified among these. The patients were enrolled in the study by consecutive sampling technique. Calculated sample size was 126; using WHO sample size calculations and keeping 20% prevalence of hyponatremia[9] in patients with hepatic encephalopathy, at 95% confidence interval and 7% margin of error.

Liver Cirrhosis was defined clinically as decrease in liver span of less than 10 cm and presence of splenomegaly and/or ascites; and on ultrasound showing increased echogenicity, altered echotexture, surface nodularity and splenomegaly or ascites. Serum sodium level was measured and <130 meq/L was defined as hyponatremia. It was further classified as mild (125-129 meql/L), moderate (116-124 meq/L) and severe (<115 meq/L). Hepatic encephalopathy was diagnosed and graded from I to IV according to the West Haven classification. Worsening of the grades of HE was considered as severity of HE[8].

Inclusion Criteria was all admitted patients of either gender above 18 years of age with established Liver Cirrhosis of any etiology; patients with HE of any grade. All those patients who were on diuretic therapy, patients with non-cirrhotic portal hypertension, patients with acute fulminant hepatitis and patients suffering from renal failure or requiring dialysis were excluded from the study. These were excluded clinically and by relevant investigations, as needed.

The study was carried out according to the principles of human research. Ethical approval of hospital ethical review board was taken. An informed verbal as well as written consent was obtained from the enrolled patients or their caregivers. Then the study patients were included from Department of Medicine of Lady Reading Hospital. Demographic details like name, hospital ID, gender, age and residential address of patients were entered in the personal data section of proforma. Detailed history and meticulous clinical examination was performed to look for signs of cirrhosis liver; presence of HE and its grading were recorded. Ultrasonography and relevant laboratory tests including serum sodium were carried out in the laboratory of Lady Reading Hospital. All the above mentioned information was recorded in pre designed proforma.

For data entry and analysis, SPSS version 21.0 was utilized. For numerical variables (age and serum sodium concentration), mean ± SD was calculated. While for categorical variables (gender, presence of hyponatremia & hepatic encephalopathy), frequencies and percentages were calculated. Hyponatremia was correlated with hepatic encephalopathy and its severity using chi square test and Spearman rank correlation test (r value calculated). Tables were used to present the data. Statistical significance was considered at p value <0.05.

RESULTS

Of the 130 patients, males were 76 (58.5%) and females were 54 (41.5%), with a ratio of 1.4:1. Mean age of study patients was 55.52 ±10.144 years (range 30-80 years).

Overall, serum sodium level was found between 113-145 meq/l; with mean values of 131.78 ±7.84. In patients with hyponatremia, it ranged from 113 to129 meq/l (mean 122.87 ±4.86).Hyponatremia was present in 48 (36.9%) patients. Among these, 26 (54.17%) were male and 22 (45.83%) were female. There were 06 patients in the age group of 30-48 years, 28 in 49-64 years and 14 in 65-80 years age group. Mild Hyponatremia was present in 12 (9.2%), Moderate in 28 (21.5%) and Severe in 8 (6.2%) patients.

Hepatic encephalopathy was present in 88 (67.7%). Hepatic encephalopathy grade I was present in 27 (20.8%), grade II in 31 (23.8 %), grade III in 16 (12.3 %), and grade IV in 14 (10.8%) patients. In 48 patients with hyponatremia, 42 were found to have HE (r =0.32, p value <0.001). Correlation of hyponatremia with HE is shown in table 1. Severity of hyponatremia and its correlation with grades of HE (r =0.33, p value <0.001) is shown in table 2.

Table 1: Hyponatremia and its correlation with hepatic encephalopathy (n=130)

Hyponatremia	Hepatic Encephalopathy		Total	Significance
	Yes	No		
Yes	42	6	48	r = 0.33 p value= <0.001
No	46	36	82	
Total	88	42	130	

Table 2: Severity of hyponatremia and its correlation with grades of hepatic encephalopathy n=130

Severity of Hyponatremia	Grades of Hepatic Encephalopathy					Total	Significance
	I	II	III	IV	None		
Mild	4	3	2	1	2	12	r = 0.33 p value= <0.001
Moderate	11	9	3	1	4	28	
Severe	1	1	3	3	0	8	
None	11	18	8	9	36	82	
Total	27	31	16	14	42	130	

DISCUSSION

In our study, the mean age was 55.52 ±10.144 years. It was similar to other published studies. In the study by Khalil et al[10], it was 57.47± 9.82 years and Khyalappa et al[11], reported mean age of study participants as 46.02±11.80 years.

In our study, Hyponatremia was present in 48 (36.9%) patients. Serum sodium level was found between 113-129 meq/l; with mean values of 122.87±4.860. It was in accordance with other studies. In a study of Egyptian hospitalized patients with liver cirrhosis by Khalil et al[10], the prevalence of hyponatremia of <130 meq/L was 45.5%, mean 123.26 ± 5.57 meq/L. In a local study from Islamabad, hyponatremia was found in 30.7% patients[8], whereas from Hyderabad Sind, its frequency was found to be 26.7%[12]. In an Italian study, prevalence of hyponatremia was 29.8%[13]. In Taiwan, cirrhotic patients with hyponatremia were found to have increased in-hospital deaths and poor survival at 6-months[14].

In the present study, hepatic encephalopathy was present in 88 (67.7%) of patients; and 42 out of 48 (87.5%) patients with hyponatremia had HE (r =0.32, p value <0.001). Hyponatremia may deleteriously affect the function of brain thereby leading to occurrence or worsening of hepatic encephalopathy[14]. Udagani et al[15] reported that hyponatremia increases the risk of neurological disorders in cirrhotic patients compared with normonatremia. In an Egyptian study, the risk for developing HE increased 2.8 fold in patients with hyponatremia, 57/91 (62.6%) patients had hepatic encephalopathy (P=0.021)[10]. In the study by Singh et al[4], 59% patients with hyponatremia were reported to have hepatic encephalopathy. On the other hand, in one study from Korea, 20.8% of patients with hyponatremia had severe complications[16].

Our results showed that severity of hyponatremia was significantly correlated with grades of hepatic encephalopathy (r =0.33, p value <0.001). According to Angeli et al[6], HE was present in 38% of the severe hyponatremic patients compared with 24% of patients with mild hyponatremia. On the other hand, those patients with normal levels of serum sodium had only 15% episode of HE. Kim et al[16] reported HE in 23% of their patients. Similarly, HE was more frequent in hyponatremic patients and the more severe the hyponatremia the greater was the grade of HE (p= 0.001) as reported in the study by Shaikh et al[12]. Moreover, the other complications of cirrhosis liver (e.g. ascites) were also found with increased frequency as the hyponatremia became severe.

These results showed that severe hyponatremia is associated with increased severity of HE[17-19]. In comparison to patients with normonatremia, patients with hyponatremia less than 130 meq/L, had higher grade of HE (p=0.011)[16]. Pathophysiologically hyponatremia and HE may be closely linked. Recent studies have suggested that hyponatremia causes low grade cerebral edema resulting in increased osmotic pressure on astrocytes leading to many neurological dysfunctions[20,21]. Moreover, there may be a significant decrease in the levels of organic osmolytes in the brain. These include myo-inositol, choline, glutamine and taurine. Both of these phenomenon depend on how severe the hyponatremia is and how acutely is the fall in the concentration of serum sodium[22,23]. Low levels of myo-inositol were related with more occurrence of HE. These changes are analogous to the presence of elevated levels of ammonia in cirrhotic patients[24,25].

CONCLUSION

Hyponatremia was found with increased frequency in patients with cirrhosis liver. It was significantly correlated with frequency and severity of hepatic encephalopathy.

RECOMMENDATIONS

Serum sodium levels should be closely monitored in patients with cirrhosis liver. Hyponatremia demands prompt diagnosis and effective therapy to prevent the incidence and severity of the cirrhosis liver related complications.

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CONTRIBUTORS

MARA conceived the idea, planned the study, and drafted the manuscript. ZA, RM and MA helped acquisition of data and did statistical analysis. MFA and ABA helped acquisition of data. IA supervised the study and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.