ORIGINAL ARTICLE

Hyponatremia – A Risk Factor for Mortality in Cirrhotics

SARAH SHOAIB QURESHI, WASIM AMER, ADNAN M JAVAID, *MEHREEN AWAIS, KHURRAM KAZMI*
Department of Medicine, Lahore Medical & Dental College/Ghurki Trust Teaching Hospital, Lahore
Correspondence to Prof. Sarah Shoaib Qureshi, Email: sarahsqureshi@yahoo.com Cell:0300-4433002

ABSTRACT:

Background; Hyponatremia is a common problem in patients with advanced cirrhosis and leads to significant morbidity and mortality in these patients.
Aim: To determine the frequency of hyponatremia in cirrhotics and in-hospital mortality in cirrhotic hospitalized patients
Methods; This was a cross sectional study conducted in inpatient medical wards and ICU of GTTH between October 1, 2019–March 31, 2020. Hyponatremia was assessed by serum sodium levels. Patient outcome at discharge was also noted. All the data was entered and analyzed using SPSS-20.
Results; in the studied 130 cases of cirrhosis 70(53.8 %) were male and 60 (46.2 %) were female patients. The mean age of my study cases was 46.71 ± 7.8 years, the mean duration of illness was 3.93 ± 1.47 years. Mean serum Sodium level was noted to be 132.45 ± 6.77 mmol/L. Hyponatremia was noted in 67 patients (51.5 %). The in hospital mortality was 18 (13.8) cases.
Conclusion; Hyponatremiais associated with significant number of cirrhotics and is associated with increased mortality in these patients.
Keywords: Liver cirrhosis, hyponatremia, sodium level.

INTRODUCTION

Cirrhosis is one of the leading cause of morbidity and mortality throughout world[1]. It is the 14th most common cause of death in the world; fourth in central Europe.[2] It is also a common cause of mortality amongst Pakistani population[3] and frequent cause of admission in our hospitals[4].According to a study 27% of hospital admission in Pakistan is due to liver disease[4] (7-25) Ten percent emergency room cases report with liver diseases. More alarming is the result that 68% of the ward admissions, and 92% of ER liver patients presented with complications of CLD. So early detection and treatment of complications of cirrhosisimproves the outcome.[5]

Hyponatremia is one of the most common electrolyte disturbance in patients with advanced cirrhosis and indicates a poorer prognosis.Hyponatremia, defined as sNa concentration ≤130 mmol/L, has a prevalence rate of 22% in cirrhotics[6]. In patients with cirrhosis, the prevalence rate of S/Na between 120 - 125 mmol/L, is 6%, and the prevalence rate of S/Na ≤120 mmol/L is 1.2%[7-9]. Hyponatremia has three clinical types: hypervolemic, euvolemic, and hypovolemic. Majority of cirrhotic patients (90%) have hypervolemic (dilutional) hyponatremia due to an increased extracellular fluid volume.Patients with cirrhosis experience reduction in effective arterial blood volume because of splanchnic arterial vasodilation as a result of increased production of nitric oxide, endotoxins, and other vasodilators[10-12]. This in turn activates the renin- angiotensin- aldosterone axis and impair free water excretion secondary to excessive antidiuretic hormone[11].In 10% cases, hyponatremia is hypovolemic[8,9], typically from over diuresis.
Hyponatremia is a marker of the severity of cirrhosis and is more prevalent in patients with Child- Pugh class C[9, 12,13]. These patients are less sensitive to diuretics and have higher hospitalization rates with complications such as spontaneous bacterial peritonitis, hepatic encephalopathy, and hepatorenal syndrome[13-15].

Early diagnosis and proper treatment can help reduce frequency of complication and mortality. The results of this study will generate current statistics and useful national database of our local population presenting to a tertiary care hospital. The study will highlight the burden of hyponatremia in cirrhosis of liver and its relation to in hospital mortality in cirrhotic patients.

The main objective of this study was to determine the frequency of in-hospital mortality in cirrhotic hospitalized patients with and without hyponatremia. Frequency of hyponatremia in cirrhotic hospitalized patients was also determined.

MATERIAL AND METHODS

This descriptive Case Series was conducted in the Department of Medicine, Ghurki Trust Teaching hospital Lahore; Tertiary care hospital during a period of 6 months from October 1, 2019–March 31, 2020. Sample size of 130 cases is calculated with 95% confidence interval, 7% margin of error and expected percentage of hyponatremia in cirrhotic hospitalized patients as 20.8%. Non probability, Consecutive sampling technique was used.

Inclusion Criteria:

- Male and female patients above the age of 18 years up to 60 years will be included.
- Patient diagnosed with given definition of cirrhosis of liver for at least 6month and admitted in ward.
- Patients having at least one serum sodium levels after admission

Exclusion Criteria:

- Patient having cardiac illness, i.e. acute coronary syndrome and cardiac failure
- Patient having cerebrovascular disease
- Patient un-willing to provide informed consent

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OPERATIONAL DEFINITIONS

Cirrhosis of liver: Cirrhosis of liver will be defined by presence of coarse parenchymal echogenicity and irregular margins on Ultrasound abdomen with Serum Albumin < 3.5g/dL, Serum Globulin >3 g/dL, and / or reversal of albumin globulin ratio to less than 1.

Hyponatremia

- Normal value of sodium is 136-145 mEq/dl.
- Mild hyponatremia is serum sodium level <135 mEq/dL.
- Moderate hyponatremia is serum sodium level <130 mEq/dL.
- Severe hyponatremia is serum sodium level <120 mEq/dL.
- Presence of mild, moderate or severe hyponatremia will be considered as presence of hyponatremia.

In-hospital mortality: It will be defined as death during hospital stay.

Data collection procedure: Consecutive patients diagnosed with cirrhosis of liver according to operational definition and fulfilling inclusion and exclusion criteria, in department of Medicine were included in the study. Informed consent was taken from each patient. Complete history and physical examination of patient was performed for all patients including duration of liver disease, history related to complications of cirrhosis. 5ml venous blood of all patients were sent to laboratory for assessment of hyponatremia (as per operational definition). The result was entered in a specially designed Performa. Patients were followed after admission till discharge or death to record in hospital mortality.

Statistical analysis: Data was entered and analyzed using computer program SPSS-17. Descriptive statistics were applied to calculate mean and standard deviation for age of the patient, duration of cirrhosis and serum sodium level. Frequencies and percentages were calculated for categorical variables like gender, hyponatremia and mortality. Both groups were compared by applying chi-square test. Effect modifiers like age, gender, duration of disease was controlled by stratification. Post stratification chi-Square test are applied to see their effect on outcome. P-Value equal or less than 0.05 is considered as significant.

RESULTS

One hundred and thirty cases of cirrhosis were included in the study. Among them 70 (53.8%) were male and 60 (46.2%) were females (Figure 1). The mean age was 46.71 ± 7.8 years (with minimum age was 22 years while maximum age was 60 years) (Table 1). None of the patient has age below 20years.

The mean duration of illness was 3.93 ± 1.47 years, minimum duration of 6 months to maximum duration 8 years and most of the patients 53 (41.8%) presented with disease duration equal/less than 3 years. Mean serum Sodium level was noted to be 132.45 ± 6.77 mmol/L, with minimum level was 110 mmol/L while maximum level was 141 mmol/L). Hyponatremia was noted in 67 patients (51.5 %) (Table 2). Mild hyponatremia was observed in 36 patients (27.7%) and moderate hyponatremia was seen in 19patients (14.6%). While only 12 patients (9.2%) had severe hyponatremia (Figure 2).

Out of total 130 patients 18 (13.8%) died in hospital and rest were discharged alive (Table 3).

In this study, 58.57% male patients had hyponatremia, while 43.33% females had hyponatremia. Hyponatremia was more frequently observed in younger patients (15 out of 16 patients between age 21-40years, while 52 out of 99 patients in age group 41-60years). It was observed that as the serum albumin level fall the severity of hyponatremia increased. Hyponatremia was equally distributed in the different groups irrespective of serum levels of globulin, aminotransferases (ALT & AST) and bilirubin. The in hospital mortality was more in hyponatremic patients than in patients having normal serum sodium levels (Table 4).

Stratification of hyponatremia with regards to age, gender and duration of disease is shown in table 5 and with regards to serum ALT, AST and bilirubin levels is shown in table 6

Mean albumin level observed was 2.72± 0.42 mg/dl, ranging from 1.9-34mg/dl. Most patients had serum albumin concentration below 2.8mg/dl (60%). Mean serum globulin concentration was 3.8±0.43 mg/dl, with range 3.1-5.1 mg/dl.

The mean value of ALT of the study cases was 51.46±20.72 U/l, the maximum value was 155 U/l, while minimum value was 31 U/l (normal range 10-50U/ml). Most of the patients had normal serum ALT levels. Mean AST concentration was 38.38± 21.0 U/l, ranging from 15-140 U/l (normal range 10-45U/ml). Serum bilirubin levels of the patients was 0.9±0.4mg/dl (normal value is upto1.1mg/dl).

Figure 1: Gender distribution.(n= 130)

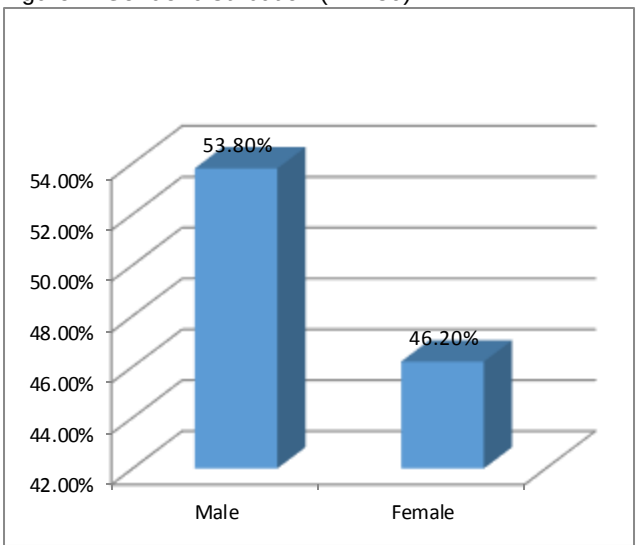

Table 1: Age wise distribution of study cases. (n= 130)

Age groups	n	%age
18-20	0	0
21-40	31	23.8
41-60	99	76.2

Table 2: Distribution of study cases by presence of hyponatremia.(n= 130)

Hyponatremia	n	%age
Yes	67	51.5
No	63	48.5
Total	130	100

Figure 2: Distribution of study cases by levels of hyponatremia (n=130)

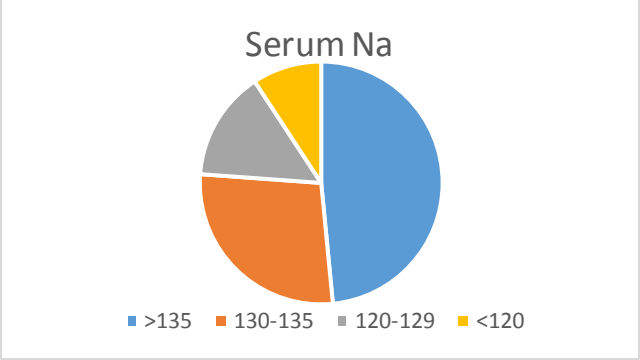

Table 3: Distribution of study cases on the basis of in hospital mortality (n= 130)

In hospital mortality	n	%age
No	112	86.2
Yes	18	13.8
Total	130	100

Table 4 Stratification of hyponatremia with regards to in hospital mortality(n= 130)

In hospital mortality	Hyponatremia		p – value
	Yes(n=67)	No(n=63)	
Yes (n=18)	16	2	0.001
No (n=112)	51	61	
Total	130		

Table 5: Stratification of hyponatremia with regards to age, gender and duration of disease

Variables		Hyponatremia		P-value
		yes (n=67)	no (n=63)	
Age groups	18-20(n=0)	0	0	0.687
	21-40(n=31)	15	16	
	41-60(n=99)	52	47	
gender	Male(n=70)	41	29	0.083
	Female(n= 60)	26	34	
Duration of disease (years)	<2 (n=14)	9	5	0.227
	2-5 (n=79)	36	43	
	>5 (n=37)	22	15	

Table 6: Stratification of hyponatremia with regards to serum ALT, AST and bilirubin levels

Variables		Hyponatremia		P-value
		Yes (n=67)	No (n=63)	
Serum ALT	Normal(n=82)	41	41	0.646
	Raised(n=48)	26	22	
Serum AST	Normal(n=95)	51	44	0.420
	Raised(n=35)	15	19	
Serum Bilirubin	Normal(n=106)	52	54	0.234
	Raised(n=24)	15	9	

DISCUSSION

Hyponatremia is a frequent finding in cirrhotics with ascites and portal hypertension. This occurs due to altered vascular resistance, especially splanchnic vascular system, and abnormal handling of sodium and water excretion by the kidney, partially due to decrease renal perfusion and partially due to hormonal changes resulting from abnormal liver functioning and decreased effective intravascular volume[16,17]. Among hormonal changes, abnormal antidiuretic hormone from the neuro-hypophysis related to circulatory dysfunction is most important[17]. The opening of portosystemic collaterals[18] and the increased synthesis of circulating vasodilators, including nitric oxide (NO), glucagon, vasoactive intestinal peptide, substance P, platelet activating factor, prostaglandins and prostacyclins play a crucial role in the pathogenesis of splanchnic vasodilation[19]. Systemic vasodilation and arterial under filling is also an important factor in development of hyponatremia[16]. Hyponatremia in a cirrhotic patient is associated with increased morbidity and mortality[16]. The degree of hyponatremia parallels the severity of the hepatic disease and is, along with the degree of sodium retention, of prognostic value. A serum sodium concentration below 130 meq/L carries a relatively poor prognosis, whereas values below 125 meq/L often indicate impending hepato renal syndrome[16]. Hyponatremia also increases the risk of complications in cirrhotic patientse, hepatic encephalopathy, SBP and ascites[20]. Hyponatremia also represents a risk factor for liver transplantation as it is associated with increased frequency of complications and impaired short-term survival after transplantation. The current standard of care based on fluid restriction is unsatisfactory. Currently, a new family of drugs, known as vaptans, which act by antagonizing specifically the effects of arginine vasopressin on the V2 receptors located in the kidney tubules, is being evaluated for their role in the management of hyponatremia[21]. The short-term treatment with vaptans is associated with a marked increase in renal solute-free water excretion and improvement of hyponatremia[21].

Our study included a total of 130 cases of liver cirrhosis meeting inclusion criteria of our study. Among them 70(53.8 %) were male patients and 60 (46.2 %) were female patients. Of these 130 study cases. Hussain et al[22] at Lahore had also reported male gender predominance over female patients which is similar to our results in his study. Khan et al[23]from Jamshoro, has also documented high male gender preponderance with 65 % male patients and Topdagi et al[24] (Turkey) has also reported male gender predominance with 58%. Zuberi et al [25] also documented 60 % male gender predominance which is in compliance with our study results. Alam et al[26] from Peshawar reported 64 % male gender preponderance which is similar to our study results.

The mean age of my study cases was 46.71 ± 7.8 years (with minimum age was 22 years while maximum age was 60 years).

Mean serum Sodium level was noted to be 132.45 ± 6.77 mmol/L, with minimum level was 110 mmol/L while maximum level was 141 mmol/L). Hyponatremia was noted in 67 (51.5 %) present study. In other studies, frequency of

hyponatremia ranges from 47-72%[23,27-29]. Khan et al [23] from Jamshoro also reported mean serum sodium level of 129.73±83.51nmol/L in patients with liver cirrhosis, which is close to our study results. Jenq et al [109] found serum sodium concentrations < 135 mEq/L in 53.2 % and ≤130 mEq/L in 28.6 %. These findings of Jenq et al [28]are in compliance with our study results. Mild hyponatremia is observed in 36(27.7%), moderate in 19(14.6%), while severe in 12 (9.2%) patients

In hospital mortality was seen in 18 (13.8) cases in this study, among them 16 patients had hyponatremia. While in a study by Zubieta-Rodriguez R[30] in hospital mortality was 23.5%, much higher than our study. In another study by Vergara et al [31] in hospital mortality is 11.6% similar to our study.

CONCLUSION

In our study, frequency of hyponatremia was very high among patients with liver cirrhosis. Hyponatremia was significantly associated with increase in mortality in cirrhotic patients. All clinicians treating such patients must monitor sodium levels for better management of cirrhotic patients as it leads to significant morbidity and mortality in these patients.

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