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ORIGINAL ARTICLE

Frequency of hyponatremia in decompensated chronic liver disease patients.

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ABSTRACT… Objectives: To find the frequency of hyponatremia in decompensated chronic liver disease patients. **Study Design:** Descriptive, Cross-sectional study. **Setting:** Department of Medicine, Bahawal Victoria Hospital, Bahawalpur, Pakistan. **Period:** October 2022 to March 2023. **Material & Methods:** A total of 118 patients of either gender aged 40-70 years having decompensated chronic liver disease were analyzed. Five ml blood was drawn under aseptic environment and was properly preserved, and sent to the hospital laboratory for analysis of sodium levels. Frequency of hyponatremia was determined and hyponatremia was labeled as serum sodium level < 130 mEq/liter. **Results:** In a total of 118 patients, the mean age was 53.69 ±7.11 years (ranging between 40-70 years) while 69 (58.5%) patients were aged between 41 to 55 years of age. There were 64 (54.2%) male and 54 (45.8%) female patients. The mean duration of chronic liver disease was 10.49±3.48 months whereas the mean BMI was 30.26±2.50 kg/m2. The mean serum bilirubin, serum globulin, serum albumin, mean albumin to globulin ratio, PT, child Pugh score and serum sodium levels were 5.43±2.41 mg/dl, 4.87±1.89 g/dl, 2.13±0.87 g/dl, 1.65±0.73, 11.33±3.41 seconds, 8.12 ± 2.68 and 118.67±9.87 mEq/liter respectively. The frequency of hyponatremia in patients with decompensated liver cirrhosis was found in 39 (33.1%) patients. **Conclusion:** This study concluded that frequency of hyponatremia in decompensated chronic liver disease patients is quite high.

Key words: Ascites, Child Pugh Class, Hyponatremia, Liver Cirrhosis, Serum Sodium.

INTRODUCTION

A variety of chronic injuries occurring from different underlying causes lead toward chronic liver disease in which irreversible scar of tissues (fibrosis) replaces the healthy liver and the function of liver progresses towards deterioration.[1] Mainly, chronic viral hepatitis (hepatitis B and C), metabolic toxicity/ induction of certain drugs and autoimmune diseases are the reasons of the cirrhosis of the liver, as a result inflammation persists and fibrosis progresses.[2,3] Moreover, liver functioning in a cirrhotic patient advances to an acute deterioration which is termed as decompensated liver disease with jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal hemorrhage as its basic characteristics.[2] Decompensated liver disease causes hospitalization more often, and for such patients, it is a serious and complex medical condition which can further extend their stay in the hospital and has 10-20% in-hospital mortality rate.[4] Such patients need to be investigated properly and managed within due course of time.[4] Higher mortality rates are observed if the development of ascites, hepatic encephalopathy, and/or gastroesophageal variceal hemorrhage are established at the onset of decompensation.[5] Aiming for an appropriate treatment, it is important to take the history, examine, and investigate the patient carefully.[4]

The development of impaired solute-free water excretion and severe sodium retention compromise the kidney function in patients of chronic liver disease.[6] Clinical complications like refractory ascites, hepatorenal syndrome and hyponatremia are significant in their association with these mechanisms and all of these contribute to raise the incidence of short-term mortality.[7] A study in 2015 reported that in decompensated

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liver disease (serum sodium ≤135 meq/L), hyponatremia was 59.46% prevalent.[8] A recently published local study shared that frequency of hyponatremia was 53.3% among patients having decompensated liver disease.[9] Many of the cirrhotic patients having hyponatremia are likely to be asymptomatic.[10] Hyponatremia is quite evident in its relation with the severity of cirrhosis. Diuretics are not effective in those patients who have both ascites and hyponatremia as refractory ascites is usually more common among them and need therapeutic paracentesis more frequently.[11] A local study performed by Shaikh S et al from Hyderabad reported the frequency of hyponatraemia as 26.7% in patients having liver cirrhosis.[12]

There are few publications in which researchers focused on decompensated liver disease, while the studies on hyponatremia in other liver conditions are widely available. If our study also manifests the same high occurrence of hyponatremia as reported in literature (59.46%8 - 70%9), then in all patients, their sodium levels need to be maintained to get assistance in curing the patients early along with standard treatment. Moreover by maintaining sodium levels, related risks of morbidity and mortality can be minimized. The objective of the study was to determine the frequency of hyponatremia in decompensated liver disease patients.

MATERIAL & METHODS

This was a descriptive cross-sectional study performed at The Department of Medicine, Bahawal Victoria Hospital, Bahawalpur, Pakistan from October 2022 to March 2023. A sample size of n=118 was calculated considering n=z2pq/d2, where z=1.96, p=26.7%14 (frequency of hyponatremia in patients with liver cirrhosis), q=100-p, d=8%, at 95% confidence level with 5% margin of error.

Inclusion criteria were both male and female patients with decompensated liver cirrhosis, aged between 40–70 years, having duration of cirrhosis more than 6 months, and Child pugh class A/B/C. Exclusion criteria were serum creatinine ≥1.5 mg/dl and those patients who were reluctant to give consent. Decompensated cirrhosis of liver was established as, if coarse parenchymal echogenicity and irregular margins & ascites on ultrasound abdomen with serum albumin < 3.5g/dl and serum globulin >3 g/dL were present. In the determination of Child-Pugh score, five clinical measures of liver disease were scored. For each measure, the given score was 1, 2 or 3, and 3 represented the most severe. Ascites and hepatic Encephalopathy severity was labeled by a consultant physician having post fellowship experience of 2 years or more, on first grand round for that patient in ward. The patients were briefed about the objectives of the study and were ensured about their provided information to be kept confidential. We also conveyed them that no risks were associated with this study. Thereafter informed and written consents from all of the patients were acquired. For study conduction, approval from Institutional Ethical Committee was also obtained.

Complete history and related information including residence, height, body mass index (BMI) and comorbidities were registered. At the time of admission, medical record was reviewed, the duration of decompensated cirrhosis of liver of each patient was noted, and the history of the use of furosemide was also taken. It was defined as YES if patient has taken oral or parenteral diuretics at any dosage in last 10 days. It was defined as NO if patient has not taken oral or parenteral diuretics at any dosage in last 10 days. We applied standard neurological examination technique for the clinical examination, more specifically for flapping tremors, disorientation in time, place or person, and coma. Serum albumin, serum globulin, albumin to globulin ratio, PT (seconds prolonged) and serum sodium were measured in the institutional laboratory. A consultant physician having at least 2 years of post fellowship experience labeled ascites and hepatic encephalopathy severity on his first grand round for that patient in the ward. Ascites was labeled as the presence of free fluid in peritoneal cavity of the decompensated liver cirrhosis patient on ultrasound abdomen.

Hepatic encephalopathy was assessed by the

presence of either of following clinical features on clinical examination: i) flapping tremors at the time of presentation in hospital, assessed by standard neurological examination techniques (flapping movement at wrist on sustained dorsiflexion), ii) disorientation in time, place or person at time of admission, assessed by standard neurological examination techniques (assessment of higher mental functions) iii) coma at time of admission (GCS ≤ 13/15). Child–Pugh score and grade were also calculated. Ascitic fluid examination was also performed for the presence of spontaneous bacterial peritonitis (either presence of >500/mm leucocytes in the ascitic fluid or presence of >250 /mm Neutrophils in the ascetic fluid were the assessment criteria). Ultrasonography of abdomen for liver status and free fluid in abdomen was done at the time of admission by a radiologist having at least one year experience in ultrasonography. Serum sodium level < 130 mEq/liter one or more times duration first 5 days of illness, was defined as Hyponatremia.

All study information was collected through a specially generated proforma.

Data analysis was carried out through "Statistical Package for Social Sciences (SPSS)", version 26.0. Quantitative variables which included age of the patient, disease duration, serum albumin, serum globulin, albumin to globulin ratio, PT (seconds prolonged), Child–Pugh score and serum sodium were expressed as mean and standard deviation. Whereas, qualitative variables like age groups, gender, hyponatremia, use of furosemide, reversal of albumin to globulin ratio (it was defined as YES if ratio of serum albumin to globulin, measured at time of admission is < 1.00, and NO if ratio of serum albumin to globulin, measured at time of admission is ≥ 1.00), Child–Pugh grades, hepatic encephalopathy and ascites were presented as frequency and percentages. Effect modifiers like age groups, gender, ascites, the use of furosemide, Child–Pugh grades, hepatic encephalopathy and spontaneous bacterial peritonitis were controlled by stratification. The effect of these effect modifiers on hyponatremia was assessed by applying post stratification chi-square test. P-value < 0.05 was considered as significant.

RESULTS

In a total of 118 patients, the mean age was 53.69 ±7.11 years (ranging between 40-70 years) while 69 (58.5%) patients were aged between 41 to 55 years of age. There were 64 (54.2%) male and 54 (45.8%) female patients. The mean duration of chronic liver disease was 10.49±3.48 months whereas the mean BMI was 30.26±2.50 kg/m2. Table-I shows details of demographic and clinical profile of patients.

Characteristics		Number (%)
Age (years)	40-55	69 (58.5%)
	56-70	49 (41.5%)
Gender	Male	64 (54.2%)
	Female	54 (45.8%)
Reversal of albumin to globulin ratio		69 (58.5%)
Child pugh class	A	30 (25.4%)
	B	44 (37.3%)
	C	44 (37.3%)
Use of furosemide		61 (51.69%)
Ascites		63 (53.39%)
Hepatic encephalopathy		43 (36.44%)
Spontaneous bacterial peritonitis		27 (22.88%)

Table-I. Demographic and clinical profile (n=118)

The mean serum bilirubin, serum globulin, serum albumin, mean albumin to globulin ratio, PT, child Pugh score and serum sodium levels were 5.43±2.41 mg/dl, 4.87±1.89 g/dl, 2.13±0.87 g/dl, 1.65±0.73, 11.33±3.41 seconds, 8.12 ± 2.68 and 118.67±9.87 mEq/liter respectively. The frequency of hyponatremia in patients with decompensated liver cirrhosis was found in 39 (33.1%) patients as shown in Figure-1. Stratification of hyponatremia with respect to study variables is shown in Table-II.

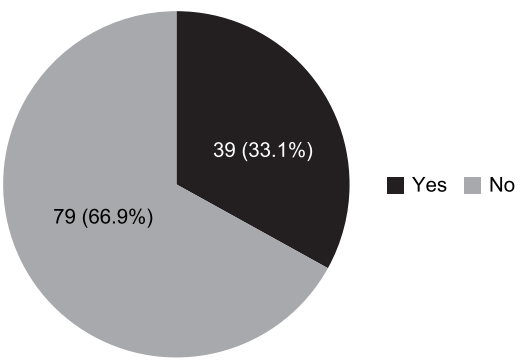

Figure-1. Frequency of hyponatremia in patients with decompensated liver cirrhosis (n=118)

Study Variables		Hyponatremia		P-Value
		Yes (n=39)	No (n=79)	
Age (years)	40-55	26 (37.7%)	43 (62.3%)	0.205
	56-70	13 (26.5%)	36 (73.5%)	
Gender	Male	19 (29.7%)	45 (70.3%)	0.398
	Female	20 (37.0%)	34 (63.0%)	
Child Pug Class	Class A	01 (3.3%)	29 (96.7%)	<0.001
	Class B	18 (40.9%)	26 (59.1%)	
	Class C	20 (45.5%)	24 (54.6%)	
Ascites		22 (34.9%)	41 (65.1%)	0.644
Use of furosemide		20 (32.8%)	41 (67.2%)	0.949
Hepatic Encephalopathy		19 (44.2%)	24 (55.8%)	0.052
Spontaneous bacterial peritonitis		08 (29.6%)	19 (70.4%)	0.667

Table-II. Stratification of hyponatremia with respect to study variables

DISCUSSION

In liver cirrhosis patients, it is very common that serum sodium concentration is reduced.[13] Although, those patients can also present hyponatremia who are with early or moderately advanced cirrhosis and according to Child-Pugh classes A and B but it is more frequent in patients with advanced disease (Child-Pugh class C).[14] Associated complications further establish the relation of hyponatremia with severity of cirrhosis.[15]

It is quite interesting that between 120 and 135 mmol/L92 serum sodium concentration values, each decreased unit increases the risk of wait-list mortality by 12% among patients planned for liver transplantation.[16] Those patients who undergo surgery and have reduced levels of serum sodium concentration are more likely to develop irreversible neurological destruction, for instance central pontine myelinolysis which occurs as a result of rapid correction of hyponatremia during early period of time after surgery.[17] Blood products are needed to be extensively used in such patients and their hospital stay also increases because in their early 30 days of transplantation, they are at higher risk of developing neurological complications, renal failure, and bacterial infections.[18] In comparison with patients in which hyponatremia is absent, hyponatremia patients are at higher risk of 3-month mortality.[18]

The frequency of hyponatremia was found to be 33.1% among patients having decompensated liver cirrhosis. Contemporary data shows that almost 50% of the patients with cirrhosis and portal hypertension have hyponatremia.[19] The "Cirrhotic Ascites Patient Population Survey (CAPPS)" analyzed 28 centers, spent 28 days to collect data of 997 patients with cirrhosis and portal hypertension of outpatient and hospitalized patients treated by hepatologists.[19] Among inpatients, hyponatremia was present in 57% and in outpatients it was 40%.[19] Another study analyzing 126 patients of liver cirrhosis admitted to intensive care unit, serum sodium concentrations < 135 mEq/L and ≤ 130 mEq/L were observed in 53.2% and 28.6% cases respectively.[20] Another study found hyponatremia to be present in 20.8% patients with liver cirrhosis.[21] Shaikh et al revealed serum sodium levels ≤ 135 mEq/L to be present among 51.6% patients of liver cirrhosis.[22]

A multi-centered study reviewed patients of liver cirrhosis and concurrent ascites and revealed that hyponatremia occurred in 49.4% patients.[23] Another study described that among inpatients with liver cirrhosis and concurrent ascites, hyponatremia was found in 29.8% (serum sodium ≤ 130 mmol/L, and had significant association with infection and ascites.[24]

Being a single center study conducted on a relatively small sample size were some of our limitations. We could not prospectively follow the impact of hyponatremia on outcomes of patients with decompensated liver disease.

CONCLUSION

This study concluded that frequency of

hyponatremia in decompensated chronic liver disease patients is quite high. Early recognition and management of hyponatremia in chronic liver disease patients should be done in order to reduce the associated morbidity and mortality.

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2	Farid ud Din	Critical revisions, Proof reading.	
3	Syed Zain Ul Abidin	Drafting.	
4	Ghulam Jilani	Data Collection, Data analysis.	
5	Muhammad Waqas Saeed	Data Collection, Literature review.