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LIVER CIRRHOSIS;
FREQUENCY AND SEVERITY OF HYPONATREMIA IN PATIENTS

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ABSTRACT… Liver cirrhosis results from prolonged, widespread but patchy hepato-cellular necrosis due to various reasons. **Objectives:** To determine the frequency and severity of hyponatremia in patients with liver cirrhosis. **Study Design:** Descriptive case series study**. Period:** Six months. **Setting:** Liaquat University Hospital Hyderabad. **Methods:** The cirrhotic subjects were assessed for hyponatremia and its severity. The data was analyzed in SPSS 16 and the frequency and percentage was calculated for hyponatremia and statistically p -value ≤0.05 was considered as significant. **Result:** Sixty five percent males and thirty five percent females of liver cirrhosis were studied. The mean age ± SD of overall cirrhotic subjects was 40.79±7.83. The hyponatremia was identified in 72% (51 males and 21 females) patients. The mean ±SD for Na+ level in overall population was 129.73±83.51 while it was 119.92±3.61 in hyponatraemic cirrhotic subjects. The sodium level in male and female hyponatraemic cirrhotic patients was 121.73±8.63 and 118.92±3.31. **Conclusions:** Dilutional hyponatremia is frequent in patients with liver cirrhosis.

Key words: Cirrhosis, hyponatremia, liver, sodium, and chronic liver disease - CLD

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INTRODUCTION

Liver cirrhosis results from prolonged, widespread but patchy hepato-cellular necrosis due to various reasons.[1] The most important classification of cirrhosis is based on etiology. The most common and important causes are alcoholic hepatic disease and chronic viral hepatitis B & C viruses. The less important causes are hemochromatosis, α1 anti trypsin deficiency, Wilson's disease, cystic fibrosis and glycogen storage disease.[1] The term compensated and decompensated cirrhosis is often used. A patient with compensated cirrhosis has no problem with regard to cirrhosis while a patient with decompensated cirrhosis either has signs of liver cell failure or complication of cirrhosis.[2]

Hyponatremia (serum Na <135 meq/L), is the most important electrolyte disorder. Its homeostasis is vital to the normal physiologic function of cells.[3-5] Identifying the etiology and risk factors for hyponatremia will help in reducing its incidence and minimize the complications associated with hyponatremia and improve the overall cost of health care. Patients with hyponatraemia have a poor survival.[6-13] There is a lack of Pakistani data on clinical spectrum of hyponatremia in cirrhosis and treatment strategies to be adapted in various clinical studies; therefore, we planned to undertake this study in patients with hepatic cirrhosis in relation to hyponatremia at our tertiary care teaching hospital.

PATIENTS AND METHODS

This descriptive case series study of six months was conducted at Liaquat University Hospital Hyderabad / Jamshoro. The inclusion criteria of the patients were liver cirrhotic subjects ≥12 years of age and of either gender whereas the exclusion criteria were the cirrhotic patients

already on diuretics therapy, the patients with hepatocellular carcinoma (HCC), patients present as syndrome of inappropriate ADH secretion (SIADH) and non-cooperative patients who didn't allow and give consent for the study. The consent was taken from patient or their attendants. Detail history was obtained; physical examination and various routine and necessary investigations were advised. The serum sodium level was determined by taking 2cc blood sample and sent to laboratory for analyses. The frequency of hyponatremia was evaulated while the cirrhosis severity by clinical and biochemical score system i.e. Child-Pugh score.[2]The normal serum sodium [Na+] level is 130-145mmol/L and the value <130 will be labeled as low or Hyponatremia.[14]The severity of hyponatremia will be categorized as: [14]130–135 mmol/L (mild), 125–130 mmol/L (moderate) and <125 mmol/L (severe). The data was entered and analyze in SPSS version 11.00. The stratification was done for qualitative and quantitative variables while the descriptive statistics were used to calculate frequency. The mean ±SD was calculated whereas the Chi-square test applied at 95% CI and statistically significance was considered when p-value was ≤0.05.

RESULTS

Total 100 cirrhotic individuals were studied for hyponatraemia. The mean age ± SD of all 100 cirrhotic subjects was 40.79±7.83. The hyponatraemia was observed in 72% (51 males and 21 females) cirrhotic subjects. The mean age ± SD was 42.71±8.72 and 40.92±8.52 (hyponatraemic males and females). The mean age ± SD was 43.82±9.73 and 41.83±7.53 (non-hyponatraemic males and females). The age in relation to gender is mentioned in Table: I while the age stratification in relation to hyponatraemia is mentioned in Table: II. The gender stratification in context to hyponatraemia is presented in Table: III whereas the sex in context to clinical and biochemical score system is displayed in Table IV. The severity of hyponatremia in relation to gender and child-pugh score is presented in Table V and VI.

The mean ± SD for BP, RR, pulse and temperature in hyponatraemic individuals was 100.00±9.42 (systolic) and 70.62±2.71 (diastolic), 19.63±0.63, 87.74±5.72 and 99.62±2.52. The mean±SD for BP, RR, pulse and temperature in non hyponatraemic cirrhotic subjects was 110.92±7.42 (systolic) and 88.41±5.31 (diastolic), 17.52±1.21, 75.83±3.11 and 98.41±1.42. The mean Na+ level in overall subjects was 129.73±83.51 while it was 119.92±3.61 in hyponatraemic cirrhotic subjects. The sodium level in male and female hyponatraemic cirrhotic patients was 121.73±8.63 and 118.92±3.31.

		GENDER		Total	P-value
	AGE	Male	Female		
	12-19	6	2	8	
		9.2%	5.7%	8.0%	
	20-29	8	11	19	
		12.3%	31.4%	19.0%	
	30-39	21	7	28	
		32.3%	20.0%	28.0%	
	40-49	22	9	31	0.05*
		33.8%	25.7%	31.0%	
	50-59	7	2	9	
		10.8%	5.7%	9.0%	
	60 +	1	4	5	
		1.5%	11.4%	5.0%	
Total		65	35	100	
		100.0%	100.0%	100.0%	

Table-I. Age in relation to gender

*statistically significant

		HYPONATREMIA		Total	P-value
	AGE	Yes	No		
	12-19	8	00	8	
		11.1%	00	8.0%	
	20-29	14	5	19	
		19.4%	17.9%	19.0%	
	30-39	22	6	28	
		30.6%	21.4%	28.0%	
	40-49	19	12	31	0.03*
		26.4%	42.9%	31.0%	
	50-59	6	3	9	
		8.3%	10.7%	9.0%	
	60 +	3	2	5	
		4.2%	7.1%	5.0%	
Total		72	28	100	
		100.0%	100.0%	100.0%	

Table-II. Age in relation to hyponatremia

Statistically significant

		HYPONATREMIA		Total	P-value
		Yes	No		
GENDER	Male	51	14	65	0.05*
		70.8%	50.0%	65.0%	
	Female	21	14	35	
		29.2%	50.0%	35.0%	
Total		72	28	100	
		100.0%	100.0%	100.0%	

Table-III. Gender in relation to hyponatremia

Statistically significant

		CHILD - PUGH CLASS			Total	P-value
		A	B	C		
GENDER	Male	18	22	11	51	0.05*
		90.0%	59.5%	73.3%	70.8%	
	Female	2	15	4	21	
		10.0%	40.5%	26.7%	29.2%	
Total		20	37	15	72	
		100.0%	100.0%	100.0%	100.0%	

Table-IV. Gender in relation child pugh

Statistically significant

		GENDER		Total	P-value
		Male	Female		
HYPONATREMIA	Mild	9	11	20	0.01*
		17.6%	52.4%	27.8%	
	Moderate	25	5	30	
		49.0%	23.8%	41.7%	
	Severe	17	5	22	
		33.3%	23.8%	30.6%	
Total		51	21	72	
		100.0%	100.0%	100.0%	

Table-V. Severity of hyponatremia in relation to gender

Statistically significant

DISCUSSION

It has shown that severity of hyponatremia associated with high complications of cirrhosis. This study evaluated the prevalence of hyponatremia and association between hyponatremia and the occurrence major complications and outcome in patients with liver cirrhosis.[15]

The present study reported 72% prevalence for hyponatremia in patients with liver cirrhosis, of which 27.8% had mild, 41.7% had moderate and 30.6 had severe hyponatremia. The study by Angeli P et al had shown 50.6% mild, 27.8% moderate and 21.6% severe hyponatremia in cirrhotic patients[16] while the study by Kim JH et al had shown 52.1% mild, 20.8% moderate and 27.1% severe hyponatremia in patients with liver cirrhosis.[17]The study published in JPMA (2010) had also shown mild, moderate and severe hyponatremia with 48.4%, 24.9% and 26.7% proportions in liver cirrhosis.[18]Borroni G et al conducted a study on hospitalized subjects with hepatic cirrhosis and according to severity of serum Na+ concentration, the severe hyponatremia was detected in 29.8% in relation to ascites.[19]

In present series the neurological impairment was observed in 40% patients whereas according to Angeli P, et al [16] the neurological impairment was present in thirty eight percent of the patients with serum sodium less than 130 meq/L. Yun BC et al (2009) showed altered sensorium in twenty three percent individuals with serum sodium less than 130 meq/L compared with fourteen percent

		CHILD - PUGH CLASS			Total	P-value
		A	B	C		
HYPONATREMIA	Mild	10	6	4	20	0.02*
		50.0%	16.2%	26.7%	27.8%	
	Moderate	5	21	4	30	
		25.0%	56.8%	26.7%	41.7%	
	Severe	5	10	7	22	
		25.0%	27.0%	46.7%	30.6%	
Total		20	37	15	72	
		100.0%	100.0%	100.0%	100.0%	

Table-IV. Hyponatremia in relation to child pugh score

Statistically significant

subjects with serum Na in a range of 131 and 135 meq/L.[20]

In present study the frequency of hepatorenal syndrome was 11/72(15%) in patient with severe hyponatremia, 07/72(9.7%) with moderate hyponatremia, 03/72(4%) with mild hyponatremia and 01/72(1.3%) with normal serum sodium concentration. Angeli P et al showed HRS in 17% patients with severe hyponatremia, ten percent patients with moderate hyponatremia and only six percent subjects with normal Na+ concentration.[16]

In present study the male population was predominant to acquire hyponatremia, the finding is consistent with the study by Xu Z et al.[21]In present series, the major presenting features identified were jaundice, abdominal distension and lower limb swelling whereas the study by Kim SH et al also identified abdominal pain, distension and jaundice as the main presenting features. [22]

Finally the study also identified that mortality is more (8.3%) in patient with moderate and severe hyponatremia whereas no death was observed in patients had normal serum sodium wit liver cirrhosis.

Hence, it has been demonstrated that hyponatremia in patients with cirrhosis is linked to impaired cerebral concentration.[23-27]In acute liver failure, the presence of low Na+ is related to brain swelling.[28]Therefore, the findings suggest that proper and appropriate monitoring of Na+ concentration is effective tool in subjects with liver cirrhosis.

CONCLUSIONS

Dilutional hyponatremia is frequent in cirrhotic patients and low Na+ concentration in hepatic cirrhosis is linked to complications of liver cirrhosis like neurological impairment, hepatorenal syndrome, osteoporosis and high morbidity and mortality. Therefore treatment of hyponatremia is important to prevent hepatic cirrhosis related complications.

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"God loves each of us as
if there were only one of us."

Saint Augustine

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2	Dr. Mukhtiar Hussain Jaffery	Drafting the article and shares its expert research opinion and experience in finalizing the manuscript	
3	Dr. Mushtaq Ali Memon	Contributed in conection and interpretation fo data and give his expert view for manuscript designing	
4	Dr. Suneel Arwani	Analysis and interpretation of data, contributed in conception and shares its expert research opinion	
5	Dr. Hamid Nawaz Ali Memon	Drafting, interpreting and analyzing data	
6	Dr. Syed Zulfiquar Ali Shah	Data collection and manuscript of data