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Original Research Paper

Medicine

PROSPECTIVE STUDY OF HYPONATREMIA IN DECOMPENSATED CHRONIC LIVER DISEASE AND ITS CORRELATION WITH SEVERITY

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ABSTRACT **Background** Hyponatremia is a key prognostic factor in patients with chronic liver disease. Cirrhotic patients may develop hyponatremia as a result of either hypovolemia (for example, diuretics) or hypervolemia. In hyponatremic cirrhotic individuals, hepatic encephalopathy, ascites, renal failure, infectious complications and pleural effusion were all much more prevalent. The aim of present study was to determine prevalence of hyponatremia and association of it with complications and final outcome in cirrhotic patients. **Methods:** Study was conducted in department of medicine, SRG Hospital and Medical College, Jhalawar. Data of patients with cirrhosis were collected prospectively. The prevalence and serum sodium levels and severity of complications of 100 patients were analyzed. Data analysis was done using licensed SPSS software version 21.0 (Chicago, Illinois). **Results:** The mean age of patients were 48.5±11.5 year. In the present study, out of 100 patients, 48 were had serum sodium level >135 meq/L and 25 were had serum sodium level < 125 meq/L. Serum sodium levels was associated strongly with the severity of liver disease as assessed by Child Pugh and MELD score. Serum sodium ≤126 indicated the existence of Ascites (p value=0.0001), hepatic encephalopathy (0.0001), hepatorenal syndrome (0.009). **Conclusions** Hyponatremia is frequent in cirrhotic patients and low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis like hepatic encephalopathy, hepatorenal syndrome and high morbidity and mortality. Treatment of hyponatremia is important to prevent possible complications of liver cirrhosis.

KEYWORDS : MELD, Cirrhosis, Hyponatremia

INTRODUCTION

One of the leading causes of death and disability around the world is cirrhosis of the liver. As a result, it places a heavy burden on the healthcare infrastructure and medical professionals in developing nations. Constipation, esophageal variceal bleed, and spontaneous bacterial peritonitis.[1-2] are all underlying conditions that can bring on HE (Hepatic encephalopathy). Hyponatremia is facilitated by systemic vasodilation and arterial underfilling in individuals with cirrhosis and portal hypertension.[2,3]

Moderate cognitive impairment, falls, seizures, coma, and death are all possible outcomes of hyponatremia in adults without cirrhosis.[4] Chronic hyponatremia from cirrhosis allows the brain to become accustomed to the low osmolality of the extracellular fluid. The severity of neurologic symptoms in patients with hyponatremia is best defined by the rate of decline in serum sodium rather than the absolute reduction in serum sodium. As a result, hyponatremia in cirrhosis patients reduces the likelihood of developing serious neurologic symptoms. However, cerebral edema and astrocyte swelling may be precipitated by hyponatremia, in addition to the astrocyte dysfunction generated by high intracellular glutamine content from ammonia metabolism.[5]

People with cirrhosis and hyponatremia have a poor quality of life because they must adhere to stringent fluid restriction. The association between hyponatremia and hepatic encephalopathy has been established.[6] Multiple studies have shown that the degree to which one experiences hyponatremia and ascites is a major predictor of disease severity and prognosis in cirrhosis.[7-9] One study demonstrated that pre-SBP serum sodium levels independently predicted SBP- related renal failure. It has been suggested that serum sodium, rather than serum creatinine, is a more sensitive and early test for diagnosing circulatorydysfunction that leads to renal failure and/or death. Patients with hyponatremia are at increased risk for hepatorenal syndrome, which is characterized by low serum sodium due to a combination of variables including lower glomerular filtration rate (GFR) and proximal salt reabsorption.[10]

Hyponatremia in cirrhosis is currently defined as a serum level of less than 130 meq/L.[11] Patients with chronic liver disease have hyponatremia as a significant prognostic factor. In addition, when compared to patients without hyponatremia, those with hyponatremia had a significantly lower chance of survival. The purpose of this research was to ascertain how common hyponatremia is in cirrhotic individuals and whether or not it is correlated with the prevalence and severity of cirrhosis.

MATERIALS AND METHODS

This descriptive cross-sectional study was carried out in the department of medicine at SRG Hospital and Medical College in Jhalawar, and it involved a total of 100 patients diagnosed with liver cirrhosis.

Sample Size –

Sample size was calculated by following method. Sample size:-

n = t2 x p x (1-p)/e2

where t = 95% confidence interval (t=1.96)

p = Proportion of Liver Cirrhosis patients among total IPD of Medicine Department SRG Hospital, Jhalawar in month of February 2020 (p = 68/1354 = 0.05022 ~ 0.05)

e = allowed error 5% (e = 0.05) putting these valuesn = (1.96)2 x 0.05 x (1-0.05) / (0.05)2

n = 72.99 ~ 73

effect of error N = n + 5% = 73 + 5% of 73 = 73 + 3.65 = 76.65 ~ 77

Now we increased the sample up to a minimum of 100 cases. .

So, minimum 100 cases of patients above 18 years with liver cirrhosis were included in the study.

Sampling Technique:
A convenient sampling technique was used to enroll the patients in study till the sample size completion and 100 patients were selected for the study.

Study Population-
All the cases of Liver cirrhosis admitted in department of medicine, SRG Hospital and Medical College, Jhalawar.

Eligibility Criteria
Inclusion criteria:
1. Patients with cirrhosis
2. Both sex included
3. Patients willing to participate in study without compulsion.

Exclusion criteria:
1. Patients with cardiac disease
2. Patients with chronic kidney disease
3. Patients on diuretics
4. Patients not willing to participate in study.

METHODOLOGY
The study was carried out after obtaining approval from the hospital's Ethical Committee. A cross-sectional study was conducted using predetermined inclusion and exclusion criteria.Patients meeting inclusion and exclusion criteria who were admitted to the General Medicine unit at Jhalawar Medical College were included. We took a complete medical history and conducted all necessary research. All patients had their serum sodium levels checked. All patients' cirrhosis severity was evaluated using the Child-Pugh score and the Model for End-Stage Liver Disease score, which were derived from the results of the investigations.

Statistical Analysis:
As a first step, we ensured that all of the questionnaires had been filled out, and we eliminated any erroneous or missing information. After making a master chart, we entered the updated data into Excel. Every ten surveys had their data entered, and then a random form was chosen to double-check the accuracy of the data. After every fifth survey was entered, an outside party checked the accuracy of the data on two randomly selected forms.

The licensed version 21.0 of SPSS was used for the data analysis (Chicago, Illinois). At first, we ran univariate analyses and used tables, text, bar-diagrams, and pie-charts to show the findings. Quantitative metrics of central tendency and dispersion were utilized to characterize continuous variables, whereas frequency counts were computed for categorical variables using descriptive statistics. Both the t-test and the analysis of variance were used to compare the continuous variables, while the chi-square test and Fisher's exact test were employed to evaluate the differences between the categorical variables. The data is shown as a mean (plus or minus the standard deviation), a count, or a percentage. To be statistically significant, the p-value has to be under 0.05.

RESULTS
There were 100 cirrhotic patients, 36 of whom were between 41 and 50 years old, and 26 who were between 51 and 60. Patients had a mean age of 48.85 11.53 years. Only 6 of the participants were female; the remaining 94 weremale. 93 patients were diagnosed with ascites, 97 with portal hypertension, 33 with HE, 24 with variceal bleed, 12 with coagulopathy, and 8 with hepatorenal syndrome. The MELD score and Child Pugh score among study participants was 21.1±8.20 and 10.2±1.88 respectively. Of all 95 cases, 95 were caused by alcohol cirrhosis, 3 by Hepatitis B, and 2 by Hepatitis C. Seven people passed away throughout the subsequent week. Table 1 shows the distribution of laboratory parameters among the study participants. The serum sodium levels of 48 people were more than 135 meq/L, while the levels of 25 people were lower than 125 meq/L. (Table 2). In our study, no statistically significant age difference was found between different group of serum sodium level.

In our study, no statistically significant gender difference was found between different group of serum sodium level. (P=0.244).

In our study, a statistically significant ascites difference was found between different group of serum sodium level. All patient who did not have ascites belonged to group 3 i.e. Serum sodium level >135 meq/L.

In our study, a statistically significant hepatic encephalopathy difference was found between different group of serum sodium level. It was present maximum in group 1 patients.

In our study, no statistically significant coagulopathy difference was found between different group of serum sodium level.

In our study, a statistically significant hepatorenal syndrome difference was found between different group of serum sodium level. It was present maximum in group 1 patients.In our study, a statistically significant difference was found in creatinine, Total bilirubin and direct bilirubin level between different group of serum sodium level. These were found to be highest in group 1.

In our study, a statistically significant difference was found in MELD and Child Pugh score between different group 1 of serum sodium level. These were found to be highest in group i.e. severe hyponatremia was found in patients with high MELD score and high CHILD PUGH SCORE

DISCUSSION
This hospital-based prospective cross-sectional study was carried out in the medicine department at the tertiary care SRG Hospital and Medical College in Jhalawar, south-east Rajasthan.

The purpose of this study was to determine the prevalence of hyponatremia and its relationships to complications and outcomes.

Patients with cirrhosis are susceptible to side effects such ascites, variceal hemorrhage, and hepatic encephalopathy (HE). The annual rate of HE growth in cirrhotic patients is about 8%. Our study examined the prevalence of hyponatremia and its connections to a number of medical problems.

25% of the patients in our study had serum sodium level below 126 meq/L. The frequency was 52% for a serum sodium cutoff value of 135meq/L. 48% of the patients had normal sodium levels. Numerous studies have revealed that hyponatremia is frequently seen in cirrhotic patients. An analogous study was conducted by Angeli P et al[1] with 997 patients from 28 sites in Europe,Asia, North and South America. According to reports, the prevalence of hyponatremia was 21.6 percent and 27.8 percent, respectively, in the sodium level 130 and 131-135meq/L groups. Lower salt levels were linked to more serious issues, harder-to-treat ascites, as well as a subpar response to medical treatment.

Sheikh et al.[12] included 217 participants in a case control study for another investigation. 58/217 people were found to have hyponatremia (26.7 percent). The remaining 48.4% of patients had normal sodium levels in their blood, whereas 54 (24.9%) patients had serum sodium levels that ranged from 131 to 135 meq/L.

On 188 individuals, Jong Hoon Kim et al.[13] conducted another investigation and discovered that 27, 20, and 52 percent of the patients had serum sodium levels of 130, 131–135, and 136 meq/L, respectively.

Hepatic encephalopathy was discovered in 76% of hyponatremia patients with blood sodium levels below 126 meq/L, in 40% of hyponatremia patients with sodium levels between 126 and 130 meq/L, and in 6% of participants with sodium levels that were normal or higher than 135 meq/L.

In another study, the percentage of hyponatremia patients with serum sodium levels below 126 meq/L who developed encephalopathy ranged from 23 to 38 percent.

Qureshi et al.[14] examined patients at the Shifa Hospital in Islamabad. In 202 individuals with cirrhosis and hepatic encephalopathy, he measured their saltlevels. A grade was given to each patient based on how severe their encephalopathy was. Patients with low sodium had a higher frequency of encephalopathy and a higher degree of encephalopathy, according to West Havens grading.

Guevera et al.[15] tracked the serum sodium levels of 61 patients over the course of a year in a prospective study. He assessed serum salt levels and looked for encephalopathy symptoms. He came to the idea that the serum sodium level may be used to predict the beginning of encephalopathy.

In cirrhosis, which is brought on by a number of mechanisms, including hyperammonemia and altered neurotransmitters, hyponatremia adds insult to the already damaged brain. Both hyponatremia and hyperammonemia cause extracellular water to be transferred into astrocytes. As a result, osmolytes drop and astrocytes grow larger. Mental sickness is the effect of this. Hyponatremia is hence a distinct risk factor for hepatic encephalopathy. Patients with low serum sodium levels, notably myoinositol, exhibited decreased intracellular osmolytes in astrocytes, according to research by Guevera et al. Hepatic encephalopathy patients have reduced myoinositol levels. This suggests a novel strategy for managing hyponatremia and shielding against hepatic encephalopathy.

20% of hyponatremia patients and 11.1% of patients with sodium levels between 126 and 135 meq/L were found to have hepatorenal syndrome; no patients with normal sodium levels did.Hepatorenal syndrome prevalence in hyponatremia patients ranged from 3.9 percent to 17 percent in other studies. Hepatorenal syndrome is more common in patients with severe hyponatremia because they have reduced effective circulatory volumes and renal perfusion. When all other protective systems have failed and salt accumulation in the kidneys continues, hepatorenal syndrome typically develops. Therefore, it becomes sense to assume that serum sodium levels fall before hepatorenal syndrome manifests. Serum sodium can therefore be used to determine the likelihood of developing renal failure up to a safe threshold.

A significant prognostic factor in those with chronic liver disease is hyponatremia. In addition, patients with hyponatremia have lower survival chances than patients without the condition.

When the death rates for the three groups were examined, 4 out of 25 hyponatremia patients, 3 out of 27 patients with sodium levels between 126 and 135 meq/L, and no patients with normal sodium all passed away. According to another study, the mortality rate for cirrhotic individuals with sodium levels < 126 meq/L was 27%. We identified a similar fatality rate during our research. In that study, the mortality rate for patients with salt levels below 125 meq/L was 48 percent. As a result, serum sodium in cirrhotic individuals correlates with morbidity and mortality and might be used as a prognostic indicator. Our results demonstrate the importance of treating hyponatremia in cirrhosis. Whenhyponatremia improves, patients no longer require rigorous fluid restrictions. Additionally, it lessens the likelihood of issues.

Table 1: Distribution of laboratory parameter among study participants

Laboratory parameter	Mean	SD	Minimum	Maximum
UREA (meq/L)	31.53	20.693	10	160
Cr (meq/L)	1.083	.8721	.3	4.8
Na (meq/L)	131.52	9.513	108	145
Total bilirubin (mg/dl)	7.630	4.0762	1.6	18.6
Direct bilirubin(mg/dl)	3.667	2.0630	.5	8.9
Total protein (mg/dl)	7.268	1.0071	4.0	9.5
Albumin (mg/dl)	2.841	.7325	1.4	4.5
AST (IU/L)	63.70	21.418	10	99
ALT(IU/L)	66.12	19.170	29	108
ALP (IU/L)	132.15	38.833	23	299
PT (sec)	28.98	13.542	11	78
INR (sec)	7.628	57.3162	.6	5.75

Table 2: Distribution of study participants according to serum sodium level

Serum sodium	Frequency	Percentage
Group 1 (< 126 meq/L)	25	25.0
Group 2 (126-135 meq/L)	27	27.0
Group 3 (>135 meq/L)	48	48.0
Total	100	100.0

Table 3: Comparison of serum sodium level with age in study participants:

Age	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
18-40 years	9	36.0%	4	14.8%	12	25.0%
41-50 years	9	36.0%	11	40.7%	16	33.3%
51-60 years	6	24.0%	9	33.3%	11	22.9%
60 years	1	4.0%	3	11.1%	9	18.8%
Total	25	100.0%	27	100.0 %	48	100.0 %

*p-value-0.399

Table 4: Comparison of serum sodium level with gender in study participants:

Gender	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Female	3	12.0%	2	7.4%	1	2.1%
Male	22	88.0%	25	92.6%	47	97.9%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.244

Table 5: Comparison of serum sodium level with ascites in study participants:

Ascites	Serum Sodium					
	<126meq/L Group 1		126-135meq/L Group 2		>135 meq/L Group 3	
	Count	%	Count	%	Count	%
Absent	0	0.0%	0	0.0%	7	14.6%
Present	25	100.0%	27	100.0 %	41	85.4%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.017

Table 6: Comparison of serum sodium level with hepatic encephalopathy in study participants:

Hepatic encephalop athy	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Absent	6	24.0%	16	59.3%	45	93.8%
Present	19	76.0%	11	40.7%	3	6.3%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.0001.

Table 7: Comparison of serum sodium level with coagulopathy in study participants:

Coagulopat hy	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Absent	20	80.0%	24	88.9%	44	91.7%
Present	5	20.0%	3	11.1%	4	8.3%
Total	25	100.0%	27	100.0%	48	100.0%

*p-value-0.342

Table 8: Comparison of serum sodium level with hepatorenal syndrome in study participants:

Hepator enal syndrom e	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Absent	20	80.0%	24	88.9%	48	100.0%
Present	5	20.0%	3	11.1%	0	0.0%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.009

Table 9: Comparison of serum sodium level with variceal bleed in study participants:

Variceal bleed	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Absent	18	72.0%	15	55.6%	43	89.6%
Present	7	28.0%	12	44.4%	5	10.4%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.142

Table 10: Comparison of serum sodium level with other laboratory parameters in study participants:

Hyponatr emia	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3		p-value
	Mean	SD	Mean	SD	Mean	SD	
Urea	38.40	33.147	33.56	20.689	26.81	7.345	0.062
Cr	1.468	1.3253	1.196	.9456	.819	.2303	0.007
Total bilirubin	10.356	2.6701	10.926	2.9916	4.356	2.2954	0.0001
Direct bilirubin	4.280	2.1527	5.230	1.7402	2.469	1.3618	0.0001
Total protein	7.264	1.1434	7.444	.8482	7.171	1.0215	0.533
Albumin	2.852	.7806	2.741	.7536	2.892	.7046	0.695
AST	66.64	22.007	64.19	19.295	61.90	22.470	0.666
ALT	64.92	17.877	61.81	20.473	69.17	18.925	0.265
ALP	127.76	39.673	139.42	43.019	130.50	36.249	0.522
PT	32.48	14.621	34.07	15.061	24.29	10.380	0.003
INR	2.080	.8935	2.152	.8206	1.3	2.7	0.611

Table 11: Comparison of serum sodium level with final outcome in study participants:

Final outcom e	Serum Sodium					
	<126 meq/L group 1		126-135 meq/L group 2		>135 meq/L group 3	
	Count	%	Count	%	Count	%
Death	4	16.0%	3	11.1%	0	0.0%
On treatment	21	84.0%	24	88.9%	48	100.0%
Total	25	100.0%	27	100.0 %	48	100.0%

*p-value-0.142

REFERENCES

1. Angeli P, Wong F, Watson H, Ginès P. Hyponatremia in cirrhosis: Results of a patient population survey. Hepatology. 2006; 44:1535–1542.
2. Abelmann WH. Hyperdynamic circulation in cirrhosis: a historical perspective. Hepatology. 1994; 20:1356–1358.
3. Groszmann RJ. Hyperdynamic circulation of liver disease 40 years later: pathophysiology and clinical consequences. Hepatology. 1994; 20:1359–1363.
4. Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med. 2000; 342:1581– 1589.
5. Ginès P, Guevara M. Hyponatremia in cirrhosis: pathogenesis, clinical significance, and management. Hepatology. 2008; 48:1002–1010.
6. Solà E, Watson H, Graupera I, Turón F, Barreto R, Rodríguez E, Pavesi M, Arroyo V, Guevara M, Ginès P. Factors related to quality of life in patients with cirrhosis and ascites: relevance of serum sodium concentration and leg edema. J Hepatol. 2012; 57:1199–1206.
7. Guevara M, Baccaro ME, Torre A, Gómez-Ansón B, Ríos J, Torres F, Rami L, Monté-Rubio GC, Martín-Llahí M, Arroyo V, et al. Hyponatremia is a risk factor of hepatic encephalopathy in patients withcirrhosis: a prospective study with time-dependent analysis. Am J Gastroenterol. 2009; 104:1382–1389.
8. Llach J, Ginès P, Arroyo V, Rimola A, Titó L, Badalamenti S, Jiménez W, Gaya J, Rivera F, Rodés J. Prognostic value of arterial pressure, endogenous vasoactive systems, and renal function in cirrhotic patients admitted to the hospital for the treatment of ascites. Gastroenterology. 1988; 94:482–487.
9. Ginés P, Quintero E, Arroyo V, Terés J, Bruguera M, Rimola A, Caballería J, Rodés J, Rozman C. Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987; 7:122–128.
10. Follo A, Llovet JM, Navasa M, Planas R, Forns X, Francitorra A, Rimola A, Gassull MA, Arroyo V, Rodés J. Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. Hepatology. 1994; 20:1495–1501.
11. John S, Thuluvath PJ. Hyponatremia in cirrhosis: pathophysiology and management. World J Gastroenterol. 2015 Mar 21;21(11):3197-205
12. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatremia and its influence on liver cirrhosis-related complications. JPMA. 2010; 60:116.
13. Kim JH, Lee JS, Lee SH, Bae WK, Kim NH, Kim KA, Moon YS- The association between the serum sodium level and the severity ofcomplications in liver cirrhosis. Korean J Intern Med. 2009 Jun;24(2):106-12.
14. Qureshi MO, Khokhar N, Saleem A, Niazi TK. Correlation of hyponatremia with hepatic encephalopathy and severity of liver disease. J Coll Physicians Surg Pak. 2014 Feb;24(2):135-7.
15. Guevara M, Baccaro ME, Ríos J, Martín-Llahí M, Uriz J, Ruiz del Arbol L, Planas R, Monescillo A, Guarner C, Crespo J, Bañares R, Arroyo V, Ginès P. Risk factors for hepatic encephalopathy in patients with cirrhosis and refractory ascites: relevance of serum sodium concentration. Liver Int. 2010 Sep;30(8):1137-42.