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Research Article

THE CORRELATION BETWEEN SERUM SODIUM LEVELS AND THE SEVERITY OF CIRRHOSIS OF LIVER AND ITS COMPLICATIONS

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ABSTRACT

Objective: The study aimed to assess the incidence of hyponatremia in cirrhosis of the liver and to evaluate the association between serum sodium levels and the severity of cirrhosis and its complications.

Methods: Data on inpatients with cirrhosis of the liver were collected on the date of admission. The serum sodium levels on day 1 and the presence of complications and their severity in 100 patients were analyzed.

Results: The incidence of dilutional hyponatremia, which was subdivided into three groups (mmol/L): A-≤130, B-131-135, and C-≥136, were 55%, 25%, and 20%, respectively. The severity of liver cirrhosis was assessed using the CTP score and the MELD score, with a higher score seen in Group A (p=0.011 and p=0.012), respectively. Furthermore in group A, higher grades of complications were seen: grade 3/gross ascites (p=0.001), grade lll/lV hepatic encephalopathy (p=0.007), spontaneous bacterial peritonitis (p=0.049), and hepatorenal syndrome (p=0.022). Even in group B with s.Na+level 131–135 mmol/L, the development of complications was no less common.

Conclusion: Serum sodium levels must be closely monitored in cirrhotic patients as they suggest the possibility of a potentially negative impact on the clinical course of the disease.

Keywords: Cirrhosis of liver, Hyponatremia, Complications.

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INTRODUCTION

A damaged liver affects almost every bodily process. "CIRRHOSIS" is defined histopathologically as the development of extensive fibrosis and the replacement of normal hepatic architecture by structurally abnormal nodules of fibrotic tissue. These structural changes lead to functional changes, collectively known as the syndrome of chronic liver failure [1]. Fibrosis and distorted vasculature eventually lead to decompensation of the liver, which is manifested by portal hypertension [2-5] and hepatocellular failure [6]. There also occurs abnormality in coagulation, hematological abnormalities, and metabolic derangements, one of its manifestations is hyponatremia. This occurs due to high serum levels of renin and aldosterone, a decreased vascular response to vasoactive drugs, and reduced solute-free water clearance (due to non-osmotic hypersecretion of antidiuretic hormone from neurohypophysis) [2,3,7-9].

Hyponatremia is a common abnormality found in approximately 57% of inpatients with chronic liver disease and in 40% of outpatients with liver disease [3,10], and is considered a key prognostic factor in cirrhotic patients. However, little is known regarding the relationship between the degree of hyponatremia and the development of complications. Therefore, this study is done to assess the incidence of hyponatremia in cirrhosis of the liver and to evaluate the association between serum sodium levels and the severity of cirrhosis of the liver and its complications.

METHODS

The study "The correlation between serum sodium levels and the severity of cirrhosis of the liver and its complications" is a single center cross-sectional study with a sample size of 100, conducted in the Medicine Department of MKCG Medical College and Hospital, Berhampur, Odisha, from September 2015 to August 2017, after seeking permission from the institutional ethical committee.

Both male and female patients aged ≥18 years with a diagnosis of cirrhosis on the basis of clinical features and ultrasound abdomen findings as per proper diagnostic criteria were included.

Patients with any liver disease other than cirrhosis were excluded. Patients on diuretics within a 1-month period before admission, other causes of hyponatremia, any history of surgery requiring the instillation of hypotonic fluids, e.g., colonoscopy preparation, transurethral resection of the prostate, etc., and the history of any chronic diseases were excluded from the study.

Based on the serum sodium levels on day 1 of admission, patients were assigned into three groups: Group A (S.Na + ≤130 mmol/L), Group B (S.Na + 131–135 mmol/L), and Group C (S.Na + ≥136 mmol/L); severity scores, that is, CTP [11] and MELD, were calculated in all three groups. Four complications of cirrhosis were looked for, namely, ascites [12,13], hepatic encephalopathy, spontaneous bacterial peritonitis, and hepatorenal syndrome in all three groups. Ascites was classified as follows: Grade 1 – ascites observed on imaging but clinically not detectable; Grade 2 – ascites easily recognized on clinical examination, treatable with a salt-restricted diet and diuretics; Grade 3-severe abdominal distension requiring LVP [14] Hepatic encephalopathy was graded as per West Haven criteria [15]. Furthermore, short-term in-hospital mortality was determined.

Statistical analysis was performed using the Statistical Package for the Social Sciences software. The statistical methods used were the Pearson Chi-square test and analysis of variance to determine the p-value for the statistical significance of S.Na+ levels with severity scores and complications of liver cirrhosis. A $p<0.05$ was considered significant.

RESULTS

Patient characteristics

One hundred consecutive patients with liver cirrhosis were assessed for severity and complications. Based on the serum sodium concentration on day 1 of admission, patients were assigned to three groups: Group A (s.Na + ≤130 mmol/L), Group B (S.Na + 131–135 mmol/L), and Group C (S.Na + ≥136 mmol/L). The number of patients in each group was 55, 25, and 20, respectively. There were no significant differences found in gender, age, or causative factors for liver cirrhosis among the three groups (age p=0.630, sex p=0.536, alcohol intake p=0.215, hepatitis B p=0.230, hepatitis C p=0.313) as shown in Table 1.

Assessment of severity scores based on serum sodium levels

Based on CTP scoring, out of 100 patients, serum levels of Groups A, B, and C were 42, 14, and 7 in CTP C (63%), 13, 11, and 12 in CTP B (36%). Thus, maximum patients were seen in serum sodium levels of ≤130 mmol/l (Group A) both in CTP scores B and C. Hence, the CTP score is significantly associated with low serum sodium levels (p=0.011), as shown in Table 2.

Based on MELD scoring (score ranges from 6 to 56), patients were classified into 5 categories: 6–16 (39%), 17–26 (34%), 27–36 (24%), 37–46 (1%), and 47–56 (2%). It signifies that in each category, the maximum number of patients fell into serum level Group A (s.Na + ≤130 mmol/l). Hence, the MELD score is found to be significantly associated with serum sodium levels (p=0.012), as shown in Table 2.

Complications developing risk in relation to serum sodium levels

The frequency and severity of complications arising in relation to serum sodium levels, ascites Grade 2 and 3 number of patients (p=0.001) (serum Na + level Group A – 16, 36; Group B-14, 4, respectively); hepatic encephalopathy Grade 3 and 4 (p=0.007) (total patient =15 and 4 in Group A, respectively); spontaneous bacterial peritonitis (p=0.049) had 19 patients in Group A; and hepatorenal syndrome (p=0.022) had 13 patients in Group A, as shown in Table 2.

Table 1: Basal characteristics of the patients (n=100)

Characteristics	Value
Gender	
Males	79
Females	21
Age	
Range in years	18–97
Etiology	
Alcohol	70
Hepatitis B	20
Hepatitis C	6
Others	4

DISCUSSION

Electrolyte disturbance occurs commonly in cirrhosis of the liver and most commonly in hyponatremia in hospitalized patients [16,17]. Hyponatremia is defined as a disorder of plasma sodium concentration of <135 mmol/L caused by abnormalities in water homeostasis [18], but in cirrhosis, it is currently defined as a serum sodium level of <130 mmol/L [18]. It has been proven, however, that even a mild decrease in serum sodium (131–135 mmol/L) carries a worse prognosis in comparison with patients within normal values [19]. Both hypovolemic and hypervolemic hyponatremia can occur in cirrhosis, but (hypervolemic) dilutional hyponatremia is seen in a larger proportion (57%) [18,20], caused by solute-free water clearance [17,21]. In recent years, hyponatremia has attracted interest as a possible prognostic factor for liver cirrhosis [22,23]. This study was conducted to examine the incidence of hyponatremia and its complications in the southern region of Odisha among patients visiting the tertiary center with liver cirrhosis.

Earlier, many studies were conducted to establish a relationship between serum sodium levels and the severity of complications. In a multicenter study comprising 997 cirrhosis patients assigned to three groups based on serum sodium levels similar to this study, 49.4% and 21.6% were in the S.Na + 131–135 mmol/L (Group B) and ≤130 mmol/L (Group A) group, respectively [6]. Similarly, in a study with 156 cirrhosis patients, 29.8% were in the S.Na + ≤130 mmol/L group, which was significantly correlated with its complications [24]. In another study consisting of 188 patients with liver cirrhosis, 47.9% and 27.1% cases were seen at S.Na + levels of 131–135 and ≤130 mmol/L, respectively [19]. In the present study, 55% and 25% of cases are seen at S.Na + levels of ≤130 and 131–135 mmol/L, respectively, which is in accordance with the earlier studies.

Studying the demographic parameters of the patients, there was no significant association between gender, age, and causative factors for liver cirrhosis among the three study groups [6,19], as indicated in Table 1. Nevertheless, this study showed that lower levels of serum sodium are significantly associated with higher CTP and MELD scores

Table 2: Severity of disease and frequency of complications by serum sodium levels

Parameter assessed	Grading	Total	GROUP A (S.Na+130 mmol/L)	GROUP B (S.Na+131–135 mmol/L)	GROUP C (S.Na + ≥136 mmol/L)	p-value
Hyponatremia			55	25	20	
CTP score	A	1	0	0	1	0.011
	B	36	13	11	12	
	C	63	42	14	7	
MELD score (score >8 indicates worse prognosis)	6–16	39	17	10	12	0.012
	17–26	34	19	9	6	
	27–36	24	16	6	2	
	37–46	1	1	0	0	
	47–56	2	2	0	0	
Ascites		94	55	24	15	0.001
	Grade 1	20	3	6	11	
	Grade 2	33	16	14	3	
	Grade 3	41	36	4	1	
Hepatic encephalopathy		40	31	6	3	0.007
	Grade 1	7	3	3	1	
	Grade 2	13	9	2	2	
	Grade 3	16	15	1	0	
	Grade 4	4	4	0	0	
Hepatorenal syndrome		15	13	2	0	0.022
Spontaneous bacterial peritonitis		25	19	3	3	0.049
Short term in-hospital mortality		13	11	1	1	0.176

(p=0.011 and 0.012, respectively) [23], indicating the presence of advanced liver disease and a poor outcome. Table 2, It was also seen that complications of cirrhosis, namely, ascites, hepatic encephalopathy, hepatorenal syndrome, and spontaneous bacterial peritonitis, occurred in greater proportion, with higher grades seen with decreasing levels of serum sodium [25]. On short-term follow-up, the overall mortality in hospitalized patients was <15%, highest with a lower serum sodium level of ≤130 mmol/L (group A) [26].

CONCLUSION

Thus, this study concludes that serum sodium levels in cirrhosis of the liver must be monitored at the time of admission, and low levels, even modest decreases, must be treated effectively. It must be considered as an effective tool in assessing the prognostic outcomes related to disease severity as well as the occurrence and severity of complications and short-term in-hospital mortality of the patients. Hence, it must be widely included in the regular protocol while assessing patients with cirrhosis of the liver.

Limitation of the study

It did not estimate the effect of serum sodium levels on the risk of developing complications but simply observed the concurrent presence of complications at the time of admission. One of the complications, i.e., bleeding manifestations, could not be assessed like in other studies done on this topic due to the lack of proper routine endoscopy procedures in the institute. Hence, further studies are needed to determine the same.

AUTHOR'S CONTRIBUTION

Dr. Rupa Pradhan, Dr. Diptimayee Tripathy, and Dr. Sibanarayan Jali were involved in the conceptualization of protocols, data collection, and research. The manuscript was finalized, edited, and submitted for publication by Dr. Rupa Pradhan.

CONFLICTS OF INTEREST

None to report.

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REFERENCES

1. Arora G, Keeffe EB. Management of chronic liver failure until liver transplantation. Med Clin N Am. 2008;839-60, ix. doi: 10.1016/j.mcna.2008.03.006, PMID: 18570945
2. Gines P, Guevara M. Hyponatremia in cirrhosis: Pathogenesis, clinical significance, and management. Hepatology. 2008 Sep;48(3):1002-10. doi: 10.1002/hep.22418, PMID: 18671303
3. Agarwal S, Thakur MB. The association between serum sodium levels and the severity of cirrhosis of liver and its complications. Indian J Appl Res. 2019;9(8). doi: 10.36106/ijar
4. Shah V. Molecular mechanisms of increased intrahepatic resistance in portal hypertension. J Clin Gastroeneterol. 2007;41(3):S259-61. doi: 10.1097/MCG.0b013e318150d0e1, PMID: 17975474
5. Treiber G, Csepregi A, Malfertheiner P. The pathophysiology of portal hypertension. Dig Dis. 2005;23:6-10. doi: 10.1159/000084720, PMID:15920320
6. Angeli P, Wong F, Watson H, Gines P, CAPPS Investigators. Hyponatremia in cirrhosis: Results of a population survey. Hepatology. 2006;44:1535-42. doi: 10.1002/hep.21412, PMID: 17133458
7. Heuman DM, Abou-Assi SG, Habib A, Williams LM, Stravitz RT, Sanyal AJ, *et al*. Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death. Hepatology. 2004;40:802-10. doi: 10.1002/hep.20405, PMID: 15382176
8. Fernandez-Esparrach G, Sanchez-Fueyo A, Gines P, Uriz J, Quintó L, Ventura PJ, *et al*. A prognostic model for predicting survival in cirrhosis with ascites. J Hepatol. 2001;34:46-52. doi: 10.1016/s0168-8278(00)00011-8, PMID: 11211907
9. Ripoll C, Banares R, Rincon D, Catalina MV, Lo Iacono O, Salcedo M, *et al*. Influence of hepatic venous pressure gradient on the prediction of survival of patients with cirrhosis in the MELD era. Hepatology. 2005;42:793-801. doi: 10.1002/hep.20871, PMid: 16175621
10. Dooley JS, Lok AS, Burroughs AK, Heathcole EJ. Sherlock's Diseases of the Liver and Biliary System. 12th ed. New Jersey: Wiley-Blackwell Publications; 2011.
11. Feldman M, Friedman LS, Brandt LJ, Sleisenger and Fordtran's Gastrointestinal and Liver Diseases: Pathophysiology/Diagnosis and Management. 9th ed. Philadelphia, PA: Saunders, Elsevier; 2010.
12. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: Part l. Diagnosis and evaluation. Am Fam Physicians. 2006;74:756-62.
13. Eisenberg RL. Gastrointestinal Radiology-a Pattern approach. 3rd ed. Philadelphia, PA: Lipincott-Raven Publishers; 1996.
14. Gines P, Angeli P, Lenz K, Moller S, Moore K, Moreau R, *et al*. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. J Hepatol. 2010;53:397-417. PMID: 20633946. DOI: 10.1016/j.jhep.2010.05.004.
15. Munoz SJ. Hepatic encephalopathy. Med Clin N Am. 2008;92:795-812, viii. doi: 10.1016/j.mcna.2008.03.009, PMID: 18570943
16. Guevara M, Gines P. Hyponatremia in liver cirrhosis: Pathogenesis and treatment. Endocrinol Nutr. 2010 May;57(2):15-21. doi: 10.1111/j.1478-3231.2010.02293.x, PMID: 20602681
17. Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342:1581-9. doi: 10.1056/NEJM200005253422107, PMID: 10824078
18. Gines P, Berl T, Bernardi M, Bichet DG, Hamon G, Jimenez W, *et al*. Hyponatremia in cirrhosis: From pathogenesis to treatment. Hepatology. 1998;28:851-64. doi: 10.1002/hep.510280337, PMID: 9731583
19. Kim JH, Lee JS, Lee SH. The association between the serum sodium level and the severity of complications in liver cirrhosis. Korean J Intern Med. 2009 Jun;24(2):106-12. doi: 10.3904/kjim.2009.24.2.106, PMID: 19543488 PMCID: PMC2698618
20. Moini M, Hoseini-Asl MK, Taghavi SA, Sagheb MM, Nikeghbalian S, Salahi H, *et al*. Hyponatremia a valuable predictor of early mortality in patients with cirrhosis listed for liver transplantation. Clin Transplant. 2011;25(4):638-45. doi: 10.1111/j.1399-0012.2010.01350.x, PMID: 21077951
21. Zameer M, Kunnathil SG, Sathar SA, Kumar A, Sreesh S, Narayanan P, *et al*. Association between serum sodium level and severity of complications of cirrhosis. 2013;3(1):S91-2. doi: 10.1016/j.jceh.2013.02.231
22. Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl. 2005;11:336-43. doi: 10.1002/lt.20329, PMID: 15719386
23. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatremia and its influence on liver cirrhosis-related complications. J Pak Med Assoc. 2010;60:116-20. PMID: 20209698
24. Borroni G, Maggi A, Sangiovanni A, Cazzaniga M, Salerno F. Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients. Dig Liver Dis. 2000;32:605-10. doi: 10.1016/s1590-8658(00)80844-0, PMID: 11142560
25. Maher M, Yosef TM, Saabry AI, Saleh SA, Alkady H. Hyponatremia and zinc deficiency as a risk factor for hepatic encephalopathy in cirrhotic patients deficiency as a risk factor for hepatic encephalopathy in cirrhotic patients. Life Sci J. 2013;10(3):1493-500.
26. Porcel A, Diaz F, Rendon P, Macias M, Martin-Herrera L, Giron-Gonzalez JA, *et al*. Dilutional hyponatremia in patients with cirrhosis and ascites. Arch Intern Med. 2002;162:323-8. doi: 10.1001/archinte.162.3.323, PMID: 11822925