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A Study of Hyponatremia in Cirrhosis of Liver and Its Prognostic Value

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Abstract
Background/Aims: *Dilutional hyponatremia associated with liver cirrhosis is caused by impaired free water clearance. Several studies have shown that serum sodium levels correlate with survival in cirrhotic patients. Little is known regarding the relationship between the degree of dilutional hyponatremia and development of cirrhotic complications. The aim of this study was to study the prevalence of hyponatremia in cirrhosis and evaluate the association between the serum sodium level and the severity of complications in liver cirrhosis and its prognostic significance.*
Methods: *It was conducted in the Department of General Medicine, PDU Medical College, Churu, Rajasthan, from Jan-2019 to Dec-2019. Data of patients with cirrhosis were collected prospectively. The prevalence and serum sodium levels and severity of complications of 100 patients were analyzed.*
Results: *The prevalence of dilutional hyponatremia, classified as serum sodium concentrations of <135 meq/L and ≤130 meqL, were 34%, 20% respectively. The serum sodium level was strongly associated with the severity of liver function impairment as assessed by Child-Pugh and MELD scores (p<0.0001). Sodium levels less than 130 meq/L indicated the existence of grade III or higher hepatic encephalopathy (OR, 10.5; CI, 3.08-35.8; p=<0.0001), Hepato-renal syndrome 15.70(95% CI=0.86-287.8; P=<0.0113). Patients with serum sodium<130meq/L had the greatest frequency of these complications, but the frequency was also increased in patients with mild reduction in serum sodium levels (131-135 meq/L).*
Conclusions: *Dilutional 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*: Hyponatremia , liver cirrhosis, hepatic encephalopathy*

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I. Introduction:

Hyponatremia is serum sodium less than 135 meq/L. Hyponatremia is the most common electrolyte disorder.[1] Its homeostasis is vital to the normal physiologic function of cells. A disturbance in body water homeostasis is a common feature of advanced cirrhosis.[1-7]This is characterized by a higher rate of renal retention of water in relation to sodium due to a reduction in solute-free water clearance. The consequent inability to adjust the amount of water excreted in the urine to the amount of water Ingested leads to dilutional hyponatremia. Hyponatremia, an excess of water in relation to the sodium in the extracellular fluid, is the most common electrolyte disorder in hospitalized patients and particularly in patients with cirrhosis.[6,7,8-16].

Clinically significant hyponatremia is relatively uncommon and is nonspecific in its presentation; therefore, the physician must consider the diagnosis in patients presenting with vague constitutional symptoms or with altered level of consciousness. 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 compared with that of patients without hyponatraemia.[11] Hyponatremia has been associated with refractory ascites, spontaneous bacterial peritonitis and hepatic encephalopathy in patients with cirrhosis. Hyponatremia can be a key prognostic factor in patients with cirrhosis of liver when it is added to MELD score. Thus, hyponatremia could be useful in predicting prognosis & development of complications in cirrhotic patients.[2]

There is a lack of Indian data on clinical spectrum of hyponatremia in cirrhosis and treatment modalities to be

adapted in various clinical studies; therefore, we planned to undertake this prospective follow-up study in patients with cirrhosis at our tertiary care centre.

II. Materials And Methods:

Place of study: The study was conducted on 100 patients admitted to Department of General Medicine, PDU Medical College, Churu, Rajasthan, from Jan-2019 to Dec-2019.

Design of the Study: The present study was a prospective observational study.

Method Of Collection Of Data: Informed consent was obtained from all patients enrolled for the study. The data of the patients was collected in a well designed proforma. The patients' demographics and the status of the patients at the time of inclusion (inpatient or outpatient) as well as severity of cirrhosis were assessed according to Child-Pugh score. A total score from 5-6, 7-9 and 10-15 was classified as class A, B and C respectively. The patients are selected based on clinical examinations, biochemical tests and ultrasound abdomen. The patients are followed over a period of one year with serum sodium levels measured at regular intervals of 3 months, 6 months and 1 year.

Inclusion Criteria: All patients with cirrhosis of liver

Exclusion Criteria: Patients with cardiac failure, chronic kidney disease**,** Patient on diuretic therapy and on drugs like SSRI,TCA, MAO inhibitors, cytotoxic drugs etc.

Data Analysis- Data was recorded as per Performa. The data analysis was computer based; SPSS-22 will be used for analysis. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. *p*-value <0.05 was considered as significant.

III. Results:

This prospective study included 100 cirrhotic patients out of which 84 (84%) males and 16(16%) females and the mean age of the patients was 44.89 10.27 years (range, 22-70years).

Table 1: Comparison of studies for prevalence of hyponatremia

Studies	Prevalence of hyponatremia (%)		
	<130 meq/L	131-135 meq/L	>135meq/L
Present study (n=100)	34% (34/100)	20% (20/100)	46% (46/100)
Angeli P et al (n=997)	21.6% (211/997)	27.8% (275/997)	50.6% (497/997)
Jong Hoon Kim et al (n=188)	27.1% (51/188)	20.8% (39/188)	52.1% (98/188)
Shaikh S (n=217)	26.7% (58/217)	24.9% (54/217)	48.4% (105/217)
Borroni G et al (n=156)	29.8% (57/156)		

Table 2: Comparison of studies on association between hepatic Encephalopathy and Serum sodium concentration

Studies	Frequency of HE		
	<130meq/L	131-135meq/L	>136meq/L
Present study (n=100)	59% (20/34)	50% (10/20)	8.7% (4/46)
Angeli P et al (n=997)	38%	24%	15%
Kim JH et al (n=188)	23%	14%	24%
Shaikh S et al (n=217)	25.8% (15/58)		

Table 3: Comparison Hepatorenal syndrome (HRS) with the serum sodium

Studies	Frequency oh HRS with serum sodium		
	<130meq/L	131-135meq/L	>136meq/L
Present study (n=100)	17.6%	15%	0%
Angeli P et al (n=997)	17%	10%	6%
Kim JH et al (n=188)	3.9%	2.5%	3%

Table 4: Association of severity serum sodium with the mortality

SERUM SODIUM	MORTALITY
<130 meq/L	8
131-135 meq/L	4
>136 meq/L	0

IV. Discussion:

Hyponatremia is an electrolyte imbalance that commonly occurs in hospitalized patients. Most cases are dilutional hyponatremia caused by the impairment of solute-free water clearance.[23] Hyponatremia resulting from the impairment of solute-free water excretion is commonly accompanied by portal hypertension.[7]Studies has shown that severity of hyponatremia associated with more complications of cirrhosis. In recent years, hyponatremia has attracted interest as a possible prognostic factor for liver cirrhosis. We conducted this prospective study to examine the prevalence of hyponatremia and association between hyponatremia and the occurrence major complications in patients with liver cirrhosis.

Angeli patel[8] conducted multi-centers study in overseas countries 997 patients with liver cirrhosis and concurrent ascites, were assigned to three groups based on serum sodium concentration, in a manner similar to that of the current study. The prevalence of hyponatremia- at serum sodium≤135meq/L, <130meq/L was 49.4%, 21.6% respectively. **(Table-1) Borroni G et al[18]** conducted a study on 156 patients hospitalized with liver cirrhosis, the prevalence of hyponatremia, based on a serum sodium concentration ≤130 meq/L, was 29.8%, and hyponatremia was significantly correlated with infection and ascites.

Shaikh S et al (2010)[19] conducted a case control study constituted 217 consecutive cirrhotic patients. Hyponatraemia (sodium <130meq/l) was present in 58/217(26.7%) patients and 54/217(24.9%) patients had serum sodiumfrom131-135 meq/lwhile105/217(48.4%) patients had serum sodium>135meq/l.

Present study the results indicate that a large proportion of patients with cirrhosis have abnormal values of serum sodium concentration. In fact, more than one half (54%) of patients with cirrhosis had values of serum sodium concentration below the normal range (<135 meq/L) and one third (34%) had values <130 meq/L. Low serum sodium levels were not associated with age, sex, or etiology of cirrhosis. Although it is generally believed that the existence of a serum sodium concentration<130meq/L is associated with difficult to treat ascites, few studies have been reported that specifically analyze the relationship between serum sodium levels and responsiveness of ascites to diuretic therapy. Arroyo et al.[3] reported that the presence of serum sodium <130 meq/L was associated with lower glomerular

filtration rate and solute-free clearance and a poorer response to diuretics compared with patients with serum sodium >130meq/L. Subsequent studies by Bernardi etal.[20] and Angeli et al.[8] showed that patients who do not respond to diuretics have lower serum sodium concentration compared with patients who respond to diuretics. The results of the current study confirm and extend these observations by showing that patients with serum sodium concentration <130 meq/l/L have a higher frequency of refractory ascites, lower response in terms of change in body weight, higher requirement of large-volume paracentesis to manage their ascites, and a shorter interval between paracentesis. Moreover, the results show that patients with serum sodium between 131 and 135mmol/L have signs of poor ascites response compared with patients with normal serum sodium concentration, although to a lesser extent than patients with serum sodium <130 meq/L.

According to Paolo Angeli hepatic encephalopathy (HE) was present in 38% of the patients with serum sodium <130 meq/l compared with 24% of patients with serum sodium between 131 and 135 meq/l and 15% of patients had serum sodium levels >135 meq/l. **Kim J Hetal (2009)[21]** showed HE was present in 23% of the patients with serum sodium <130 meq/l compared with14% of patients with serum sodium between 131 and 135 meq/l and 24% of patients had serum sodium levels >135 meq/l.

Shaikh S et al (2010)[19] showed hepatic encephalopathy was present in 26/217 (11.9%) patients, of which 15/58(25.8%) patients were with serum sodium<130meq/l **(Table-2)**

In present study the frequency of hepatic encephalopathy was associated with serum sodium levels in such a way that patients with serum sodium <130 meq/l had 20/34 (59%) of hepatic encephalopathy compared to patients with normal serum sodium concentration4/46(8.7%).Patients with serum sodium between131and135 meq/l had a lower frequency of encephalopathy 10/20 (50%) compared to patients with serum sodium <130meq/l.

In present study the frequency of hepatorenal syndrome was 6/34 (17.6%) in patient with serum

sodium <130 meq/L compared to three patient (15%) with serum sodium131-135meq/L and none with normal serum sodium concentration.

Angeli Petals[8] showed HRS in17% patients with serum sodium<130meq/L compared with 10% in patients with serum sodium 130-135meq/L and only 6% in patients with normal serum sodium concentration.

Kim JH et al (2009)[21] showed HRS in 17% patients with serum sodium<130meq/L compared with 10% in patients with serum sodium 130-135meq/L and only 6% in patients with normal serum sodium concentration. (**Table 3**)

In the present study there was no association found between serum Sodium and Gastrointestinal Bleeding and coagulopathy; similar result shown by Angeli Petal[8] and Shaikh S et al[19].

Finally our study also indicates that mortality is more in patient with low serum sodium compared to normal serum sodium concentration. 12 patient died in group had serum sodium<135meq/L and no death in patients with normal serum sodium.(**Table 4**)

V. Conclusion:

Dilutional hyponatremia is frequent in cirrhotic patients and low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis Like hepaticencephalopathy, hepatorenal syndrome and high morbidity and mortality. Treatment of hyponatremia is important to prevent possible complications of liver cirrhosis.

Conflict Of Interest: there is no conflict of interest between authors.

References:

[1]. Epstein M. Derangements of renal water handling in liverdisease. Gastroenterology. 1985; 89:1415-1425.
[2]. Arroyo V, Claria J, Salo J, Jime´nez W. Antidiuretic hormone and the pathogenesis of water retention in cirrhosis with ascites. Semin Liver Dis.1994;14:44-58.
[3]. Gine`sP,AbrahamW,SchrierRW.Vasopressininpathophysiologicalstates. SeminNephrol.1994; 14:384-397.
[4]. HeckerR, SherlockS. Electrolyte and circulatory changes interminal liver failure. Lancet 1956;271:1121-1125.
[5]. ShearL, Hall P W 3rd, Gabuzda G J. Renal failure in patients with cirrhosis of the liver. II. Factors influencing maximal urinary flow rate. Am J Med. 1965; 39:199-209.
[6]. Arroyo V, Rodes J, Gutierrez-Lizarraga MA. Prognostic value of spontaneous hyponatremia in cirrhosis with ascites. Dig Dis Sci. 1976; 21:249-256.
[7]. Gine`sP,BerlT,BernardiM,BichetDG,HamonG,JimenezW,et al. Hyponatremia in cirrhosis: from pathogenesis to treatment. HEPATOLOGY. 1998; 8:851-864.
[8]. AngeliP,WongF,WatsonH,GinesP.Hyponatremiaincirrhosis:resultsof a patient population survey. Hepatology. 2006;44:1535-1542.
[9]. Heuman DM, Abou-Assi SG, Habib A, Williams LM, Strawitz RT, Sanyal AJ et al. Persistent ascites and low serum sodium identify patientswith cirrhosis and low MELD scores who are at high risk for early death. Hepatology. 2004; 40:802-810.
[10]. Mónica Guevara, María E. Baccaro, Jose Ríos, Marta Martín-LlahI, Juan Uriz, Luis Ruiz del Arbol et al. Risk factors for hepatic encephalopathy in patients with cirrhosis and refractory ascites: relevance of serum sodium concentration. Liver International.2010;30:1137-42
[11]. Fernandez-Esparrach G, Sanchez-Fueyo A, Gines P, Uriz J, Quint L,VenturaPJetal.Aprognosticmodelforpredictingsurvivalincirrhosiswith ascites. J Hepatol.2001;34:46-52
[12]. Ripoll C, Banares R, Rincon D, Catalina MV, Lo lacono O, Salcedo M etal. Influence of hepatic venous pressure gradient on the prediction of survival patients with cirrhosis in the MELDEra.Hepatology.2005;42:793-801
[13]. LlachJ,GinesP,ArroyoV,RimolaA,TitoL,BadalamentiSetal. 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
[14]. Gines P, Quintero E, Arroyo V, Teres J, Bruguera M, Rimola Aetal. Compensated cirrhosis: natural history and prognostic factors. Hepatology. 1987; 7:122-128.
[15]. Cosby RL, Yee B, Schrier RW. New classification with prognostic value in cirrhotic patients. Miner ElectrolyteMetab.1989;15:261-266
[16]. RobertsonGL,BerlT.Pathophysiologyofwatermetabolism:waterretaining disorders. In: Brenner BM, editor. The Kidney. 8th ed. Philadelphia:Saunders;2007:873-928.
[17]. Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342:1581- 1589.
[18]. Borroni, G., Maggi, A., Sangiovanni, A., Cazzaniga, M, Salerno F. Clinical relevance of hyponatraemia for the hospital outcome of cirrhotic patients. Digestive and Liver Disease. 2000; 32:605–610.
[19]. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. JPMA. 2010;60:116.
[20]. Bernardi M, LaffiG,SalvagniniM,AzzenaG,BonatoS,MarraF,et al. Efficacy and safety of the stepped care medical treatment of ascites in liver cirrhosis: a randomized controlled clinical trial comparing two diets with different sodium content. Liver 1993; 13:156-162.
[21]. Jong Hoon Kim, June Sung Lee, Seuk Hyun Lee, Won Ki Bae, Nam-Hoon Kim, Kyung-Ah Kim, et al. The Association Between The Serum Sodium Level And The Severity Of Complications In Liver Cirrhosis. Korean J Intern Med.2009 Jun; 24(2): 106–112.

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