International Journal of Research in Health and Allied Sciences
Journal home page: www.ijrhas.com
Official Publication of "Society for Scientific Research and Studies" [Regd.]
ISSN: 2455-7803

ORIGINAL RESEARCH

Study and prognostication of hyponatremia in hepatic encephalopathy of chronic liver disease

Shubham Malani[1], Prasanna Kumar Satpathy[2], Shubham Agrawal[1], Sreekar Sura[1], Bharath Gowda[1]

[1]Resident, [2]Professor, Department of General Medicine, Dr. D. Y. Patil medical college, hospital and research centre, Pimpri, Pune

ABSTRACT:
Background: Chronic liver disease (CLD) is a pathologic entity characterized by continuous advancing worsening of hepatic functions for a minimum of six to seven months. Hepatic encephalopathy (HE) is a rescindable group of pathologies manifesting in the form of impairment in brain function, occurring in subjects with progressive hepatic failure. Hyponatremia is one of the commonest electrolyte dysfunction problem found to be significantly prevalent among hospitalized subjects. Hence; the present study was undertaken for assessing the prognostication of hyponatremia in hepatic encephalopathy of chronic liver disease. **Materials & methods:** 50 consecutive patients with Hepatic Encephalopathy due to Chronic Liver Disease were enrolled. A detailed clinical history was taken of all the patients and/or relatives regarding the etiology of the disease which included the patients suffering from existing liver disease for more than 10 years and known cases of Chronic Liver Disease for more than 6 months with abnormal LFT were selected. Sodium levels were assessed and incidence of hyponatremia was evaluated. SPSS software was used for evaluation of level of significance. **Results:** Hyponatremia was found to be present in 30 percent of the patients (3 patients) with grade I Hepatic encephalopathy, 27.27 percent of the patients (3 patients) with grade II Hepatic encephalopathy, 69.23 percent of the patients (9 patients) with grade III Hepatic encephalopathy and 81.25 percent of the patients (14 patients) with grade IV Hepatic encephalopathy. Significant results were obtained while assessing the occurrence of hyponatremia in difference grades of hepatic encephalopathy. While analyzing the correlation between sodium levels and severity of hepatic encephalopathy, significant results were obtained. Mean sodium levels among patients with Grade I HE, grade II HE, Grade III HE and Grade IV HE was found to be 139.41 mEq/L, 140.14 mEq/L, 133.40 mEq/L and 131.0 mEq/L respectively. 20 percent of the patients with Child Pugh Score A, 23.8 percent of the patients with Child Pugh score B and 91.97 percent of the patients with Child Pugh score C had hyponatremia. While analyzing the correlation between sodium levels and severity of hepatic encephalopathy, significant results were obtained. **Conclusion:** Hyponatremia is a common feature in patients with hepatic encephalopathy and its severity increased with its increasing grade of severity of disease. Close monitoring of serum sodium concentration should be performed in patients with cirrhosis in order to prevent the rapid development of cirrhosis related complications.
Key words: Hyponatremia, hepatic encephalopathy, Hyponatremia

Received: 8 October, 2020 Accepted: 27 October, 2020

Corresponding author: Dr. Shubham Malani, Resident, Department of General Medicine, Dr. D. Y. Patil medical college, hospital and research centre, Pimpri, Pune

This article may be cited as: Malani S, Satpathy PK, Agrawal S, Sura S, Gowda B. Study and prognostication of hyponatremia in hepatic encephalopathy of chronic liver disease. Int J Res Health Allied Sci 2020; 6(6):1-5.

INTRODUCTION

Chronic liver disease (CLD) is a pathologic entity characterized by continuous advancing worsening of hepatic functions for a minimum of six to seven months. The altered variable includes dysfunction of clotting factor's synthesis, dysfunction of protein formation process, alteration in the detoxification activity of harmful metabolic products and bile excretion dysfunction.[1]

Hepatic encephalopathy (HE) is a rescindable group of pathologies manifesting in the form of impairment in brain function, occurring in subjects with progressive hepatic failure. It is also known as portosystemic encephalopathy (PSE). The physiologic variation occurring in serum sodium levels in healthy subjects ranges between 135 mEq/L to 145 mEq/L. Its homeostasis is essentially required for adequate functioning of a tissue/organ (cellular level). Any disturbance in the levels and balance in the regulation of complete body water can result in significant alterations in sodium levels. Decompensated chronic liver disease

(DCLD) is correlated with dysfunction in water homeostasis resulting in to dysnatremias.[2, 3]

Hyponatremia is one of the commonest electrolyte dysfunction problem found to be significantly prevalent among hospitalized subjects. In liver cirrhosis patients, Hyponatremia is presently identified as a serum sodium level of less than 130 meq/L.[4]

In portal hypertension patients also, occurrence of hyponatremia is also a common phenomenon occurring because of activation of antidiuretic hormone that transpires after the reduction in effective arterial volume in relation to splanchnic arterial vasodilation. However; chronic hyponatremia results in exhaustion of intracellular organic osmolytes. Myoinositol is one such osmolye which regulates intracellular water. Osmolytes present in astrocytes delivers a cellular defense against intracellular swelling and hence, can quickly accumulate or deplete as per osmotic sensors. Indeed, data from previous literature have shown that hyponatremia is a crucial diagnostic and prognostic marker for occurrence of overt HE in liver cirrhosis patients.[5- 7]

Hence; under the light of above mentioned data, the present study was undertaken for assessing the prognostication of hyponatremia in hepatic encephalopathy of chronic liver disease.

MATERIALS & METHODS

The present study was undertaken for assessing the prognostication of hyponatremia in hepatic encephalopathy of chronic liver disease. 50 consecutive patients with Hepatic Encephalopathy due to Chronic Liver Disease were enrolled. Cases are drawn from general medicine ward & MICU from D.Y.Patil hospital and research centre. Ethical approval was obtained from institutional ethical committee and written consent was obtained from all the patients after explaining in detail the entire research protocol.

Inclusion Criteria

- Patients of age more than 18 years.
- Confirmed cases of hepatic encephalopathy of chronic liver disease by clinical and lab investigations.

Exclusion Criteria: Patients with

- Head injury
- CNS tumor
- Subarachnoid Hemorrhage
- Neurotuberculosis
- HIV with CNS involvement
- Meningitis
- Encephalitis
- Other hypovolemic and hypervolemic states

A detailed clinical history was taken of all the patients and/or relatives regarding the etiology of the disease which included the patients suffering from existing liver disease for more than 10 years and known cases of Chronic Liver Disease for more than 6 months with abnormal LFT with the following features were selected for the study -

Grades of Hepatic encephalopathy-

- Grade I- Sleep reversal pattern, mild confusion, irritability, flapping tremors.
- Grade II- lethargy, disorientation, inappropriate behavior, Tremors.
- Grade III- Somnolence, severe confusion, aggressive behavior, Asterixis.
- Grade IV- Coma.

Patients were clinically examined for features of Chronic Liver Disease, Portal Hypertension & Hepatic Encephalopathy. Complete haematological and biochemical examination of all the patients was carried out. SPSS software was used for evaluation of level of significance. Chi-square test and student t test were used for evaluation of level of significance.

RESULTS

Mean age of the patients was 58.68 years. 84 percent of the (42 patients) were males while the remaining were females. Alcohol was the main etiologic factor found to be present in 76 percent of the patients (38 patients) while viral etiology of cirrhosis of liver was found to be present in 14 percent of the patients (4 patients). Icterus, male pattern baldness and fetor hepaticus was found to be present in 72 percent, 22 percent and 46 percent of the patients respectively. Out of 50 patients, hyponatremia was found to be present in 56 percent of the patients (28 patients). Hyponatremia was found to be present in 30 percent of the patients (3 patients) with grade I Hepatic encephalopathy, 27.27 percent of the patients (3 patients) with grade II Hepatic encephalopathy, 69.23 percent of the patients (9 patients) with grade III Hepatic encephalopathy and 81.25 percent of the patients (14 patients) with grade IV Hepatic encephalopathy. Significant results were obtained while assessing the occurrence of hyponatremia in difference grades of hepatic encephalopathy. While analyzing the correlation between sodium levels and severity of hepatic encephalopathy, significant results were obtained. Mean sodium levels among patients with Grade I HE, grade II HE, Grade III HE and Grade IV HE was found to be 139.41 mEq/L, 140.14 mEq/L, 133.40 mEq/L and 131.0 mEq/L respectively. 20 percent of the patients with Child Pugh Score A, 23.8 percent of the patients with Child Pugh score B and 91.97 percent of the patients with Child Pugh score C had hyponatremia. While analyzing the correlation between sodium levels and severity of hepatic encephalopathy, significant results were obtained.

Table 1: Incidence of hyponatremia (Na levels < 135 mEq/L) in Hepatic encephalopathy patients

Parameter	Hyponatremia
Number of patients	28
Percentage of patients	56

DISCUSSION

One of largest organ of human body is Liver. At the same time, it is also a complex organ acting as a site and scaffold for occurrence of numerous functional and productive activities of human body. In the field of health care, Chronic parenchymal hepatic disease is routinely encountered. Portal hypertension is accountable for maximum amount of adverse events that streak the alterattion from compensated to decompensated cirrhosis.

Table 2: Incidence of hyponatremia in different grades of Hepatic encephalopathy patients

Grade of hepatic encephalopathy	Hyponatremia present		Hyponatremia absent		Total	
	Number of patients	Percentage	Number of patients	Percentage	Number of patients	Percentage
Grade I	3	30	7	70	10	100
Grade II	3	27.27	8	72.73	11	100
Grade III	9	69.23	4	30.77	13	100
Grade IV	13	81.25	3	18.75	16	100
Total	28	56	22	44	50	100
Chi-square value	13.871					
p- value	0.0030 (Significant)					

Table 3: Correlation of sodium levels and severity of hepatic encephalopathy

Serum sodium levels (mEq/L)	Grade I and Grade II		Grade III and Grade IV	
	Number	Percentage	Number	Percentage
≤125	1	4.77	5	17.24
126 to 130	2	9.52	8	27.59
131 to 135	3	14.29	9	31.03
136 to 145	8	38.09	5	17.24
≥146	7	33.33	2	6.89
Total	21	100	29	100
Chi-square value	11.75			
p- value	0.019 (Significant)			

Graph 1: Mean sodium levels among patients divided on the basis of different grades of hepatic encephalopathy

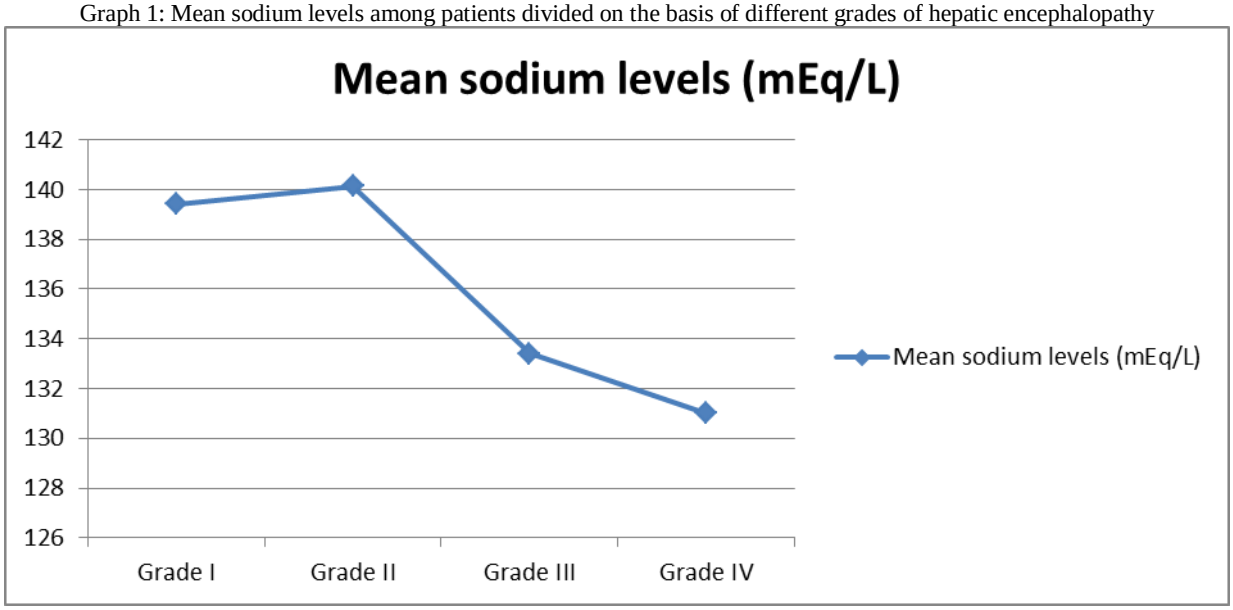

Table 4: Incidence of hyponatremia among patients according to severity of cirrhosis of liver

Child Pugh score	Hyponatremia present		Hyponatremia absent		Total	
	Number of patients	Percentage	Number of patients	Percentage	Number of patients	Percentage
A	1	20	4	80	5	100
B	5	23.8	16	76.2	21	100
C	22	91.67	2	8.33	24	100
Total	28	56	22	44	50	100
Chi-square value	27.143					
p- value	0.0000 (Significant)					

Table 5: Comparison of serum ammonia, bilirubin, albumin and PT/INR in patients with and without hyponatremia

Parameter	Hyponatremia present		Hyponatremia absent		p- value
	Mean	SD	Mean	SD	
S. Ammonia	155.08	49.38	105.45	40.41	0.000
Bilirubin	2.28	0.46	2.27	0.62	0.010
Albumin	2.79	0.32	3.13	0.33	0.040
PT/INR	2.27	0.47	1.78	0.43	0.002

Severe hyponatremia, and decreased arterial pressure are clinical findings seen in patients with advanced cirrhosis. Hyponatremia is categorized by excessive retention of water in kidneys relative to sodium as a result of reduced solute-free water clearance. Hyponatremia might be cuased for numerous factors associated to cirrhosis and portal hypertension. In relation ot hyponatremia and hepatic encephalopathy, there are no particular clinical parameters linking the two conditions.

In the present study, 20 percent of the patients (10 patients) and 22 percent of the patients (11 patients) had Grade I and Grade II encephalopathy respectively, while 26 percent of the patients (13 patients) and 32 percent of the patients (16 patients) belonged to Grade III and Grade IV of hepatic encephalopathy respectively. Similar results have been reported in the past literature. Bashir et al, in their study reported that frequency of stage of disease was recorded as 17(14.78%) had grade 1, 36(31.30%) had grade 2, 24(20.87%) had grade 3 while 38(33.05%) had grade 4. In aonther study conducted by Javed M et al, authors reported that out of 132 patients with hepatic encephalopathy, 21.21 %, 22.73%, 22.73% and 33.33 % patients were had Grade I, II, III and IV HE respectively. Memon MA et al, conducted a study on cirrhosis of liver patients with HE and reported that 37.5%, 12.5% 18.8% and 31.2% of the patients had Grade I, II, III and IV hepatic encephalopathy respectively.[7, 8, 11]

Mean sodium levels among Hepatic encephalopathy patients was found to be 135.32 (+ 10.08) mEq/L. Similar range of serum sodium levels have been reported in the past studies on HE patients. In the studu conducted by Bashir et al, mean sodium level among patients with HE was found to be 132.42 nEq/L.Javed M et al, in another study reported that 42.4% of the patients, 35.6 percent of the patients, 21.2 percent of the patients and 0.8 percent of the patients with HE had sodium levels of more than 135 mEq/L, between 131-135mEq/L, between 125-130 mEq/L and less than 125 mEq/L respectively.[7, 11]

Out of 50 patients, hyponatremia was found to be present in 56 percent of the patients (28 patients). Similar higher prevlance of hyponatremia has been reported in HE patients with cirrhosis of liver in the past studies. Javed M et al[11] reported the presence of Hyponatremia in 57.6% of patients with HE, while Sulehria SB et al[12] reported that 129 (51.6%) patients had hyponatremia due to chronic liver disease.

Hyponatremia was found to be present in 30 percent of the patients (3 patients) with grade I Hepatic encephalopathy, 27.27 percent of the patients (3 patients) with grade II Hepatic encephalopathy, 69.23 percent of the patients (9 patients) with grade III Hepatic encephalopathy and 81.25 percent of the patients (14 patients) with grade IV Hepatic encephalopathy. Mean sodium levels among patients with Grade I HE, grade II HE, Grade III HE and Grade IV HE was found to be 139.41 mEq/L, 140.14 mEq/L, 133.40 mEq/L and 131.0 mEq/L respectively. Significant results were obtained while assessing the occurrence of hyponatremia in difference grades of hepatic encephalopathy. Hence; incidence of hyponatremia increases with increasing severity grade of HE in cirrhosis of liver patients. Our results were in concordance with the results obtained in previous studies where authros have also demonstrated similar findings. In a previous study conducted by Kim JH et al, out of 50 liver cirrhosis patients with presence of HE, 72 percent of the patients had sodium levels of less than 135 mEq/L, 28 percent of the patients had sodium levels of more than 135 mEq/L, 28 percent of the patients. They also obtained significant results while analysing the correlation of severity of HE with sodium levels.[13]

Qureshi et al, in their study, observed that hyponatremia was present in 65.79 percent of the patients with moderate to severe HE while it was present in only 48.39 percent of the patients with HE. They also reported significantly higher prevalence of hyponatremia in patients with higher severe grade of HE.[14] Sulehria SB et al reported that out of 129 patients with hyponatraemia, 16 (12.4%) were having grade I, 24 (18.6%) had grade II, 38 (9.46%) had grade III and 51 (39.54%) had grade IV hepatic encephalopathy.[12]

20 percent of the patients with Child Pugh Score A, 23.8 percent of the patients with Child Pugh score B and 91.97 percent of the patients with Child Pugh score C had hyponatremia. While analyzing the correlation between sodium levels and severity of hepatic encephalopathy, significant results were obtained. Our results were in concordance with the results otbained by previous authors who have also demonstrated similar findings in their respective studies. Majoirty of the patients with severe hyponatremia, in the study conducted by Qureshi et al, belonged to Child Pugh class C. Javed M et al also observed significant correlation .i.e. increasing incidence of hyponatremia with increasing seveity of HE. In aonther study condcucted by Rekha NH et al, authors reported significant lower levels of serum sodium in patients with increasing grades of liver cirrhosis.[11, 14, 15] Kim JH et al, in their study, observed significantly higher associated of Hyponatremia with increased severity of liver disease (as evaluated by Child-Pugh and MELD scores).[13]

CONCLUSION

Hyponatremia is a common feature in patients with hepatic encephalopathy and its severity increased with its increasing grade of severity of disease. Close monitoring of serum sodium concentration should be performed in patients with cirrhosis in order to prevent the rapid development of cirrhosis related complications.

REFERENCES

1. Sharma A, Nagalli S. Chronic Liver Disease. [Updated 2020 Jul 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554597/
2. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician. 2006 Sep 01;74(5):756-62.
3. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, et al. Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. PLoS One. 2017;12(10):e0187033.
4. Ferenci P. Hepatic encephalopathy. Gastroenterol Rep (Oxf). 2017;5(2):138-147.
5. Mandiga P, Foris LA, Kassim G, et al. Hepatic Encephalopathy. [Updated 2020 Jun 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430869/
6. Rathi S, Chopra M, Chouduri G, et al. Prevalence of Minimal Hepatic Encephalopathy in Patients With Liver Cirrhosis: A Cross-Sectional, Clinicoepidemiological, Multicenter, Nationwide Study in India: The PREDICT Study. J Clin Exp Hepatol. 2019;9(4):476-483.
7. Bashir S, Pervaiz A, Khan HA et al. Frequency of Hyponatremia in Patients with Hepatic Encephalopathy at a tertiary care hospital. PJMHS. 2019; 13(2): 306- 308.
8. Memon MA, Memom N, Qadir A, Dal AS. Association of Hyponatremia and Encephalopathy in Patients with Chronic Liver Disease. Annals. 2017; 23(1): 48- 51.
9. Parry CD, Patra J, Rehm J. Alcohol consumption and non-communicable diseases: epidemiology and policy implications. Addiction. 2011;106(10):1718-1724.
10. Mokdad AA, Lopez AD, Shahraz S, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med. 2014;12:145.
11. Javed M, Saleem K, Baig FA, Nida M. Correlation of Serum Ammonia and Serum Sodium Levels with Grade of Hepatic Encephalopathy in Patients with Cirrhosis of Liver. Proceeding S.Z.P.G.M.I. 2016; 30(2): 83-88.
12. Sulehria SB, Zafar MS, Rauf, M, Ghafoor A. Frequency of Hyponatraemia in Hepatic Encephalopathy in Chronic Liver Disease at Mayo Hospital, Lahore. PJMHS. 2013; 4: 1204-6.
13. Kim JH, Lee JS, Lee SH, et al. The association between the serum sodium level and the severity of complications in liver cirrhosis. Korean J Intern Med. 2009;24:106–112
14. Qureshi MO, Khokhar N, Saleem A, Niazi TK. Correlation of Hyponatremia with Hepatic Encephalopathy and Severity of Liver Disease. Journal of the College of Physicians and Surgeons Pakistan 2014, Vol. 24 (2): 135-137
15. Rekha NH, Sajila N. Clinical study on correlation between serum sodium levels and serum ammonia levels in relation with hepatic encephalopathy in patients with cirrhosis of liver. IAIM, 2019; 6(12): 40-46.