Association of Hyponatremia and Encephalopathy in Patients with Chronic Liver Disease

Muhammad Akbar Memon,1 Nadeem Memom,2 Abdul Qadir,3 Abdul Salam Dal4

Abstract

Objective: To determine the association of hyponatremia in chronic liver disease patients with presentation of hepatic encephalopathy (HE) at Isra university Hospital Hyderabad.

Methods: This study was cross sectional and carried out at medicine and gastroenterology department of Isra university Hospital Hyderabad and MMC Mirpur-Khas. Study duration was from September 2015 to March 2016. All the cases with age more than 25 years, both genders after diagnosis of chronic liver disease with sign and symptoms of Hepatic Encephalopathy were selected in this study. Blood sample for serum sodium level, was send to diagnostic laboratory of the hospital. Hyponatremia was classified as: 130–135 mEq/L (mild), 125–130 mEq/L (moderate) and < 125 mEq/L (severe). Hepatic encephalopathy was categorized according to the West Haven classification (4 grades)

Results: Total number of cases was 80. Mean age was 48 + 8.5 years. 55 (68.5%) patients were male. Majority of cases, 55 (68.5%) patients were infected with HCV. 40% patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia. On the grading of encephalopathy, 30 (37.5%) patients had grade 1 encephalopathy while 25/(31.2%) patients had grade 2, 15/(18.8%) had grade 3 while 10 (12.5%) patients hade grade 4. The serum sodium levels significantly decreased with increasing severity of hepatic encephalopathy (P = 0.001).

Conclusion: We concluded that the hyponatremia is significantly linked with Hepatic Encephalopathy (HE) in patients having chronic liver disease (CLD).

Key Words: CLD, hyponatremia, hepatic encephalopathy.

Introduction

Chronic liver diseases (CLD) and its complications are the major health problem, due to big burden of Hepatitis C virus and Hepatitis B virus in the community1 and it is also the commonest reason of death in Pakistani population. It is very common reason of admission to our hospitals.2 In the decompensation condition, cases having CLD generally present with ascites, jaundice, portal hypertension, gastrointestinal hemorrhage, spontaneous bacterial peritonitis and hepatic encephalopathy.3 About 30% of patients with CLD usually die due to Porto systemic encephalopathy.4 The clinical course of patients with CLD is frequently complicated due to increase in the renal function abnormalities and imbalance of electrolytes.5

In the body disturbance of the water is the main sign of advance cirrhosis.6 This phenomena of distur-
Bance of water is linked to the existence of ascites and is characterized by the development of dilutional hyponatremia, which is a frequent complication and sequel of chronic liver disease.\(^5\,^7\) Recent study indicates that hyponatremia is a key prognostic factor in patients with CLD.\(^5\) The prevalence of hyponatremia [serum Na < 130 mEq/L] in patients with cirrhosis with ascites is approximately 30%.\(^9\) The relationship between hyponatremia and severity of cirrhosis is associated with the development of complications, hepatic encephalopathy, hepatorenal syndrome and spontaneous bacterial peritonitis are more presented in cases having serum concentration < 130 mEq.\(^10\) Furthermore in cases having ascites, those having hyponatremia have a lower diuretics response, higher frequency of refractory ascites, and frequent requirement of the therapeutic paracentesis.\(^11\) A study from Pakistan demonstrated 51.6% of CLD cases had serum sodium concentration below than the normal level.\(^5\) Borroni et al.\(^12\) reported that hyponatremia was in 30% of CLD cases. Hyponatremia can induce or aggravate Hepatic encephalopathy, leading to disease progression like seizures, coma and even brain death. The aim of this study was to evaluate the association of hyponatremia in chronic liver disease patients with presentation of hepatic encephalopathy.

**Material and Methods**

This study was cross sectional and carried out at medicine and gastroenterology department of Isra university Hospital Hyderabad and MMC Mirpur Khas. Study duration was 7 months from September 2015 to March 2016. All the cases with age more than 25 years, both genders, after diagnosis of chronic liver disease with sign and symptoms of hepatic encephalopathy were selected in this study. All the cases on diuretic therapy, with hepatocellular carcinoma, with diabetes, hypertension (HTN), heart failure and chronic kidney disease (CKD) were excluded from the study. Detailed history, clinical examination and various routine and necessary investigations were done in all cases. After that blood sample for serum sodium level, was sent to diagnostic laboratory of the hospital. The demographic profile of the patients was noted. The severity of decrease sodium concentration was assessed as normal serum sodium [Na+] level is 135-145mmol/L and the value < 135 was labeled as low or hyponatremia. The severity of hyponatremia was categorized as: 130–135 mEq/L (mild), 125–130 mEq/L (moderate) and < 125 mEq/L (severe). The hepatic encephalopathy was graded according to the West Haven classification (4 grades). Grades I-II were taken as mild to moderate encephalopathy, while grades III-IV were taken as severe encephalopathy. All the data regarding age, gender, serum sodium concentration, presence of hepatic encephalopathy were recorded. All the data were entered into SPSS 16.0 version and were analyzed by using the same software.

**Results**

Total number of cases was 80. Mean age was 48 ± 8.5 years. Males were found in the majority as compared to females. Regarding virology status of cases, HCV patients were most common, 10 patients had HBV while 15 patients were infected by both HCV and HBV (Table 1).

**Table 1: Basic characteristic of cases (n = 80).**

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of Patients/(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (mean ± SD)</td>
<td>48.4 ± 8.5 years</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>55 (68.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>25 (31.5%)</td>
</tr>
<tr>
<td>Virology</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>55 (68.5%)</td>
</tr>
<tr>
<td>HBV</td>
<td>10 (31.5%)</td>
</tr>
<tr>
<td>HCV + HBV</td>
<td>15 (31.5%)</td>
</tr>
</tbody>
</table>

**Fig. 1: Hyponatremia Classification n = 80.**
According to classification of hyponatremia, majority of the patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia (Fig. 1).

On the grading of encephalopathy, mostly patients were found with grade 1 encephalopathy while 25 patients had grade 2, 15 patients had grade 3 while 10 patients had grade 4 encephalopathy (Fig. 2).

In the results of this study serum sodium level significantly increased with increasing the severity of hepatic encephalopathy $p = value 0.001$ (Table 3.)

**Discussion**

Hepatic encephalopathy (HE) is commonest and serious complications of cirrhosis and is also the main reason of mortality.\(^{13}\) Hyponatremia can induce or aggravate HE, leading to disease progression and even death.\(^{14,15}\) In this study total number of cases was 80. Mean age was 48 ± 8.5 years. 55 (68.5%) patients were male while 25 (31.5%) patients were female. Similarly Qureshi MA et al.\(^{16}\) reported that of 202 patients, 90 (44.6%) were males and 112 (55.4%) females. Eighty-one (40.1%) patients were of the age greater than 60 years. Sulehria SB et al.\(^{17}\) reported that of 129 patients, 172 (68.8%) were male and 112 (31.2%) were female.

In this study 40% patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia. As well as Sulehria SB et al.\(^{17}\) reported that 129 patients had hyponatremia due to chronic liver disease, while 121 (48.4%) had no hyponatremia. In a Korean study\(^{18}\) prevalence of hyponatremia (less than serum sodium ≤ 135 mmol/L) was 47.9% in hospitalized patients.

The hyponatremia sodium (≤ 130 mmol/L was 27). 1%. In this series on the grading of encephalopathy, 30 (37.5%) patients had grade 1 encephalopathy while 25 (31.2%) patients had grade 2, 15 (18.8%) had grade 3 while 10 (12.5%) patients had grade 4 encephalopathy. Sulehria SB et al.\(^{17}\) reported that out of 129 patients with hyponatremia, 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.

In the results of this study decreases of serum sodium level is very important in CLD and its severity is significantly associated with severity of hepatic encephalopathy $p = value 0.001$. Similarly Samiullah Shaikh et al.\(^{19}\) stated that the greater frequency of hyponatremia was seen in patients having hepatic encephalopathy. In another study, the severity of hyponatremia, particularly at sodium level ≤ 130 mmol/L, corresponded to increase the risks of ascites, hepatic encephalopathy and other complications of cirrhosis, as compared those with the serum sodium level ≤ 136 mmol/L.\(^{15,20}\)

Association between HE and serum sodium levels may be described as; severe liver failure in cases with level of serum sodium < 130 meq/l, and these both events may be pathophysiologically associated.\(^{21}\) Decreased sodium level in cases having CLD, is associated with are marked reduction of organic osmolytes in the cerebral concentration, that probably reflect compensatory osmo regulatory mechanisms against cell swelling.\(^{22,23}\)

**Conclusion**

We concluded that the hyponatremia is significantly associated with hepatic encephalopathy in patients having chronic liver disease. Therefore it is recom-

**Table 2: Grading of Hepatic Encephalopathy (n = 80).**

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade: I</td>
<td>30</td>
<td>37.5%</td>
</tr>
<tr>
<td>Grade: II</td>
<td>25</td>
<td>12.5%</td>
</tr>
<tr>
<td>Grade: III</td>
<td>15</td>
<td>18.8%</td>
</tr>
<tr>
<td>Grade: IV</td>
<td>10</td>
<td>31.2%</td>
</tr>
</tbody>
</table>

**Table 3: Hyponatremia According to Severity of Hepatic Encephalopathy (n = 80).**

<table>
<thead>
<tr>
<th>Encephalopathy</th>
<th>Normal N = 32</th>
<th>Mild N = 20</th>
<th>Moderate N = 16</th>
<th>Severe N = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade: I</td>
<td>20</td>
<td>07</td>
<td>03</td>
<td>00</td>
</tr>
<tr>
<td>Grade: II</td>
<td>11</td>
<td>08</td>
<td>05</td>
<td>01</td>
</tr>
<tr>
<td>Grade: III</td>
<td>01</td>
<td>04</td>
<td>05</td>
<td>05</td>
</tr>
<tr>
<td>Grade: IV</td>
<td>00</td>
<td>01</td>
<td>03</td>
<td>06</td>
</tr>
</tbody>
</table>

$P = value 0.001$ by applying the chi-square test
mended that every patient who presents with chronic liver disease should be investigated for hyponatremia to identify patients at high risk of complications including hepatic encephalopathy.

References


