



CODEN [USA]: IAJPBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF  
**PHARMACEUTICAL SCIENCES**

Available online at: <http://www.iajps.com>

Research Article

**RELATIONSHIP AMONG HEPATIC ENCEPHALOPATHY (HE)  
AND HYPONATREMIA IN CLD PATIENTS**

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Article Received: October 2019 Accepted: November 2019 Published: December 2019

**Abstract:**

**Objective:** To determine the association of hyponatremia in chronic liver disease patients with presentation of hepatic encephalopathy (HE).

**Study design:** A cross sectional study.

**Methods:** This study was cross sectional and carried out at medicine and gastroenterology department of Nishtar hospital, Multan. Study duration was from October, 2018 to September, 2019. 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 had grade 4. The serum sodium levels significantly decreased with in- creasing 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.

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Please cite this article in press Muhammad Nauman Rasheed et al., *Relationship Among Hepatic Encephalopathy (HE) And Hyponatremia In CLD Patients.*, Indo Am. J. P. Sci, 2019; 06(12).

**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 community [1] 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 disturbance 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 [8]. 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 Pakis- tan 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 Nishtar hospital, Multan. Study duration was from October, 2018 to September, 2019. 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.

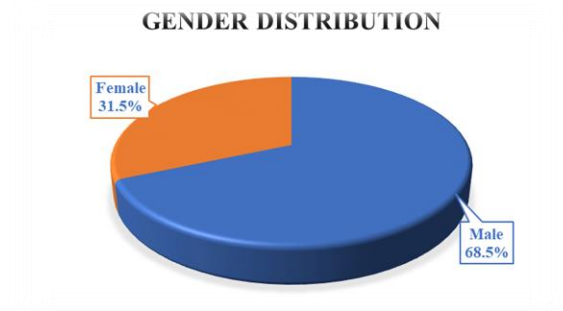
The demographic profile of the patients was noted. The severity of decrease sodium concentration was assessed as normal serum sodium [Na+] level is 135-145mmol/L and the value < 135 was labeled as low or hyponatremia. The severity of hyponatremia was categorized as: 130–135 mEq/L (mild), 125–130 mEq/L (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 was recorded. All the data were entered into SPSS version 20 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 No 01: Basic Characteristic of Cases**

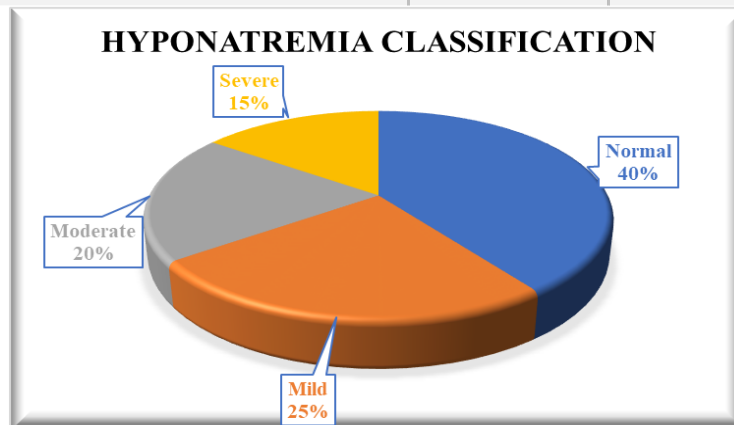
Variables		Qty	%age
Age (Mean±SD)		48.4 ± 8.5 years	
Gender	Male	55	68.75%
	Female	25	31.25%
Virology	HCV	55	68.75%
	HBV	10	12.50%
	HCV+HBV	15	18.75%



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 (Table 2).

**Table No 02: Hyponatremia Classification**

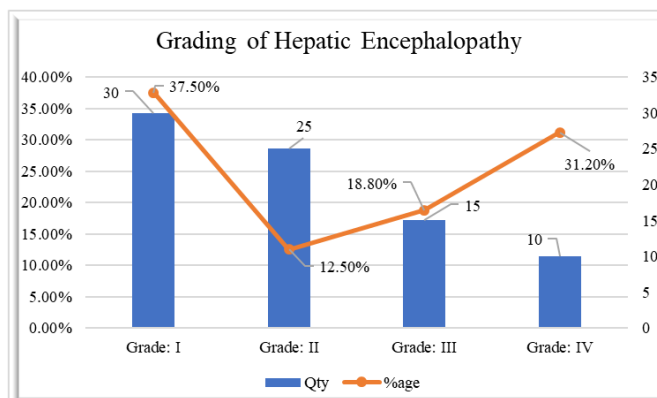
Classification	Qty	%age
Normal	32	40%
Mild	20	25%
Moderate	16	20%
Severe	12	15%
<b>Total</b>	<b>80</b>	<b>100%</b>



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 (Table 3).

**Table No 03: Grading of Hepatic Encephalopathy**

VARIABLES	QTY	%AGE
GRADE: I	30	37.5%
GRADE: II	25	12.5%
GRADE: III	15	18.8%
GRADE: IV	10	31.2%



In the results of this study serum sodium level significantly decreased with increasing the severity of hepatic encephalopathy p value = 0.001 (Table 4).

**Table No 04: Hyponatremia According to Severity of Hepatic Encephalopathy**

Encephalopathy	Severity of Hyponatremia			
	Normal	Mild	Moderate	Severe
Grade: I	20	07	03	00
Grade: II	11	08	05	01
Grade: III	01	04	05	05
Grade: IV	00	01	03	06
<b>Total</b>	32	20	16	12

## DISCUSSION:

Hepatic encephalopathy (HE) is commonest and serious complications of cirrhosis and is also the main reason of mortality [13]. Hypo- natremia 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  $48 \pm 8.5$  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 common age was recorded  $44.56 \pm 3.63$  years, 172 (68.8%) were male and 78 (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 (51.6%) 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  $\leq 135$  mmol/L) was 47.9% in hospitalized patients. The hyponatremia sodium ( $\leq 130$  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 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.

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 hypo- natremia, particularly at sodium level  $\leq 130$  mmol/L, corresponded to increase the risks of ascites, hepatic encephalopathy and other complications of cirrhosis, as compared those with the serum sodium level  $\leq 136$  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 mark able 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 recommended 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.

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