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Hypokalemia and Hyponatremia in Hepatic Encephalopathy and Its Distribution Across Age, Gender, and Grade of Hepatic Encephalopathy

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ABSTRACT

Hepatic encephalopathy is a complication of cirrhotic liver disease precipitated by a variety of factors. One such factor is disturbance in the levels of sodium and potassium. **Objectives:** To determine the prevalence of hypokalemia and hyponatremia in patients of hepatic encephalopathy at a secondary care setting and its distribution in different age groups, gender, and grades of hepatic encephalopathy. **Methods:** This cross-sectional descriptive study with stratified analysis was held at the Department of Medicine, Tehsil Headquarter Hospital, Sarai Alamgir, Pakistan, from January 2024 to February 2025. In this study, a total of 127 patients who presented with hepatic encephalopathy were included. All these patients were assessed for the presence of hypokalemia and hyponatremia. **Results:** Mean age of hepatic encephalopathy sufferers was 50.64 ± 10.29 years. There were 87 (68.50%) male and 40 (31.50%) female patients. The most common cause of cirrhotic liver disease was the hepatitis C virus found in 62 (48.80%) patients. Prevalence of hypokalemia and hyponatremia in HE patients was 24 (18.90%) and 49 (38.60%), respectively. There was no significant difference in the prevalence of hypokalemia in age groups (p=0.609), gender (p=0.482), or grades of hepatic encephalopathy (p=0.902). Hyponatremia was significantly higher in older people (p=0.005) while there was no significant difference in its prevalence based on gender (p=0.824) or hepatic encephalopathy grade (p=0.621). **Conclusions:** Hypokalemia and hyponatremia are highly common in patients with hepatic encephalopathy presenting at a secondary care hospital.

INTRODUCTION

Cirrhotic liver disease (CLD) is a major global cause of morbidity and mortality [1]. Globally, this condition has been reported to have an incidence of 58.4 million [2]. In Pakistan, the exact incidence of this condition is not known; however, it has been found that the most common cause of this condition in the Pakistani population is hepatitis C infection, with a frequency of 47.6% [3]. Several complications can complicate the course of this chronic disease, including ascites, tremors, jaundice, bleeding, bruising, gynecomastia, multi-organ failure, cryoglobulinemia, and hepatocellular carcinoma [4]. Another important complication of this condition is hepatic encephalopathy (HE), with a reported prevalence of 40% [5]. Patients with CLD are at risk of electrolyte disturbance due to a low salt diet, laxative use leading to recurrent diarrhea, and use of diuretics [6]. These disturbances can occur in almost all the electrolytes, but the most important ones are hypokalemia and hyponatremia, which in severe cases can be life-threatening due to their related neurologic and cardiac complications. [7, 8]. In previous literature, the prevalence of hyponatremia among patients with HE has been reported at 36.9% [9]. Similarly, in one study that included patients with HE, upon analysis of the presence of hypokalemia, it was found that the prevalence of this electrolyte disturbance was 30% [10].

When it comes to the prevalence of aforementioned electrolyte disturbances, results are primarily from high-

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output tertiary care centers, where mostly complicated cases are referred, which may add bias to their results. In addition, most of the patient burden is catered to at secondary care hospitals as these are more accessible to the community and are usually the first places where patients present. Despite this, no such data regarding dyselectrolytemia is available from secondary healthcare centers. This study aims to determine the frequency of hypokalemia in patients with HE presenting at a secondary care hospital in Pakistan.

METHODS

This descriptive analytical study was conducted at the Department of Medicine, Tehsil Headquarter Hospital, Sarai Alamgir, Pakistan, from January 2024 to February 2025 after obtaining approval from the ethical committee (Ref no: EC/001/02/). Sample size of 127 was calculated using WHO sample size calculator (developed by K. C. Lun, Peter Y. W. Chiam and Chuah Aaron of the W.H.O. Collaborating Centre for Health Informatics and the Medical Informatics Program of the National University of Singapore) by assuming confidence level of 95%, absolute precision of 8% and anticipated frequency of hypokalemia in patients of HE of 30% [10]. Patients who were between 25 and 75 years, who were either male or female, had CLD and presented in the Emergency Department with the diagnosis of HE was included. Patients who had concomitant chronic renal failure, acute fulminant hepatitis, hypoglycemia, diabetic ketoacidosis, hyperglycemic hyperosmolar state, stroke, and uremic encephalopathy were excluded. The study population was selected by using a non-probability consecutive sampling method. A written consent, which was signed by the study participants, was made an essential prerequisite. Baseline characteristics, including age, gender, duration of CLD, cause of CLD, and grade of HE based on West Haven criteria, were documented. Grade 0 or minimal HE (impaired neuropsychological functions that could only be assessed by the means of test but no clinically overt change in mental state of the patient), Grade 1 HE (minimal degree of lack of awareness, feelings of anxiety, poor and shorter span of attention, euphoria and impairment of ability to add or subtract), Grade 2 HE (apathic patient with symptoms of lethargy, change in personality of the patient, behavioral alterations and being disoriented in time), Grade 3 (excessive sleepiness, stupor but intact ability to respond to stimulus, severe disorientation and confusion) and Grade 4 (coma) [11]. After that, patients were assessed for the presence of hypokalemia and hyponatremia by taking a blood sample of 5ml, placing it in the serum vial, and sending the sample to the laboratory. Hypokalemia was defined as serum potassium levels < 3.5meq/l. Hyponatremia was defined as serum sodium levels < 135 meq/l.

Statistical analysis of the collected data was performed by using Statistical Package for Social Sciences, IBM SPSS version 22:00, Armonk, New York, USA. Quantitative data (age and duration of CLD) were represented using the mean with standard deviation. Qualitative data (gender, cause of CLD, grade of HE, hypokalemia, and hyponatremia) were represented by using percentages and frequency. Stratification of the prevalence of hypokalemia and hyponatremia was based on age, gender, and grade of HE, and post-stratification comparative analysis was done using the Chi-square test. A p-value of ≤0.05 was statistically significant.

RESULTS

In this study, the mean age of HE sufferers was 50.64 ± 10.29 years. There were 87 (68.50%) male and 40 (31.50%) female patients. Mean duration of CLD was 4.71 ± 2.50 years. The most common cases of CLD were HCV found in 62 (48.80%) patients, followed by NAFLD in 16 (12.60%), HBV in 15 (11.80%), and alcohol use in 13 (10.20%) patients. Demographic characteristics of patients with HE is given in table 1.

Table 1: Demographic Characteristics of Patients with HE (n=127)

Characteristic	Mean ± SD; n (%)
Age	
Years	50.64 ± 10.29
Gender	
Male	87 (68.50%)
Female	40 (31.50%)
Duration of CLD	
Years	4.71 ± 2.50
Cause of CLD	
HCV	62 (48.80%)
HBV	15 (11.80%)
NAFLD	16 (12.60%)
Alcohol Use	13 (10.20%)
No Cause Identified	21 (16.50%)
Grade of HE	
1	34 (26.80%)
2	30 (23.60%)
3	32 (25.20%)
4	31 (24.40%)

SD = Standard deviation, CLD = Cirrhotic liver disease, HCV = Hepatitis C virus, HBV = Hepatitis B virus, NAFLD = Non-alcoholic fatty liver disease, HE = Hepatic encephalopathy

Prevalence of hypokalemia and hyponatremia in HE patients was 24 (18.90%) and 49 (38.60%), respectively. In the younger age group (n=42), the prevalence of hypokalemia and hyponatremia was 9 (21.43%) and 9 (21.43%), while in the older age group (n = 85), it was 15 (17.65%) (p=0.609) and 40 (47.06%) (p=0.005), respectively. Stratification of the prevalence of dyselectrolytemia based

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on age is demonstrated in table 2.

Table 2: Stratification of Prevalence of Dyselectrolytemia in HE Patients Based on Age (n=127)

Age Stratification	< 45 Years (n=42)	≥ 42 Years (n=85)	p-value[a]
Hypokalemia	9 (21.43%)	15 (17.65%)	0.609
Hyponatremia	9 (21.43%)	40 (47.06%)	0.005

In male patients (n=87), the prevalence of hypokalemia and hyponatremia was 15 (17.24%) and 33 (37.93%), while in female patients (n=40), it was 9 (22.50%) (p=0.482) and 16 (40.00%) (p=0.824), respectively. Stratification of the prevalence of dyselectrolytemia based on gender is demonstrated in table 3.

Table 3: Stratification of Prevalence of Dyselectrolytemia in HE Patients Based on Gender (n=127)

Age Stratification	Male (n=87)	Female (n=40)	p-value[a]
Hypokalemia	15 (17.24%)	9 (22.50%)	0.482
Hyponatremia	33 (37.93%)	16 (40.00%)	0.824

Across different grades of HE, there was no significant difference in the prevalence of hypokalemia (p=0.902) and hyponatremia (p=0.902). Stratification of the prevalence of dyselectrolytemia based on grade of HE is demonstrated in table 4.

Table 4: Stratification of Prevalence of Dyselectrolytemia in HE Patients Based on Grade of HE (n=127)

Grade of HE Stratification	1 (n=34)	2 (n=30)	3 (n=32)	4 (n=31)	p-value[a]
Hypokalemia	6 (17.65%)	7 (23.33%)	6 (18.75%)	5 (16.13%)	0.902
Hyponatremia	11 (32.35%)	14 (46.67%)	11 (34.38%)	13 (41.94%)	0.621

HE = Hepatic encephalopathy, a = Chi-square test, b = Pearson chi-square test

DISCUSSION

HE is a life-threatening complication of the CLD, which is characterized primarily by impaired cognition and higher motor functions [12, 13]. The present study focused on an important aspect of this complication, i.e., hypokalemia and hyponatremia. The average age of the HE sufferers was 51 years. Similar to this, a study was conducted with a different aim in which patients suffering from HE was included; in this study, the average age of HE sufferers averaged between 48 and 52 years [14]. Proportion of male patients was higher than female patients with males making up 68.5% of the study population, thereby, exhibiting a male to female ratio of 2.2:1. Similar to this, a large-scale epidemiological survey revealed that at global scale, men were affected more from this chronic liver condition as compared to females with the incidence of CLD in both genders reported at 1.2 and 0.8 million, respectively [15]. In another study, a similar male predominance was reported in terms of having CLD [16]. The reason for this male predominance can be attributed to higher chances of men to indulge in activities (like shaving outside, smoking, outdoor dining, and exposure to quack treatment) that can result in exposure to common causes of CLD. In the present study, the most common cause that led to the development of CLD was chronic viral hepatitis C infection. The reason for this trend could be attributed to the fact that HCV is highly prevalent in the Gujrat district of Pakistan, where this study was conducted. [17] This finding was congruent with what was described in a study conducted by Gonzalez-Chagolla *et al.* who stated that among all the factors that contribute to the etiology of CLD and cirrhosis, hepatitis C is a major contributor. [18] Contrarily, this was not the case in a global epidemiological survey conducted by Zhang *et al.* in which it was reported that although hepatitis C does contribute to the etiology of this progressive condition, major contributor to the rising prevalence of this progressive damage to the liver is now NAFLD which may be due to rising number of people across the globe who are becoming overweight and obese [19]. In this study, the prevalence of hypokalemia and hyponatremia in patients presenting with HE was 18.9% and 38.6%, respectively. Compared to this, a study found that the prevalence of hypokalemia among patients presenting at various tertiary care institutions across the globe with this complication of CLD was 35%, which was relatively higher than the present study [20]. In another study, conducted on a much larger scale, hypokalemia prevalence was even higher compared to the present study and was reported at 78% [21]. In one study, HE patients presenting at a tertiary care center were analyzed for the presence of dyselectrolytemia, and it was reported that the prevalence of deficient levels of sodium and potassium in these patients was 75% and 50%, respectively, with both proportions significantly higher compared to the present study [22]. Similarly, in another study, hyponatremia prevalence among HE patients presenting at a tertiary care hospital was reported at 58.28% [23]. Such major difference in the prevalence being reported in previous studies and what has been observed in present study could have occurred due to the differences in sample sizes, type of treatment being used by the patients (particularly the doses of laxatives and diuretics), level of disease awareness and dietary restrictions to be followed, progression of CLD, HE severity pattern and level of healthcare facility of presentation. Upon stratification of the prevalence of hyponatremia and hypokalemia by age, it was observed that there was no significant difference based on hypokalemia prevalence among age groups (p=0.609), but the prevalence of hyponatremia was significantly higher among HE patients who were in the older age group (p=0.005). One possible reason for higher hyponatremia prevalence in older patients could be

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attributed to the physiological decline in kidney function as well as the use of medications that can alter sodium balance, both of which are common in older age [24]. Upon gender stratification of hyponatremia and hypokalemia, it was observed that there was no significant difference between male and female patients based on the prevalence of hyponatremia (p=0.482) or hypokalemia (p=0.824). This demonstrates that gender does not play any role in determining the occurrence of dyselectrolytemia in HE patients. Similarly, it was observed that there was no statistically significant association between HE severity (based on West Haven criteria) and prevalence of either hyponatremia (p=0.621) or hypokalemia (p=0.902). Based on the findings of the present study, it is evident that hypokalemia and hyponatremia are highly prevalent among CLD patients presenting with HE at a secondary care hospital, but as compared to those who were analyzed at tertiary care and teaching hospitals, this prevalence is relatively low. This indicates that patients may have dyselectrolytemia even at earlier stages of disease, where they are mostly managed at secondary care hospitals, and thus, this screening should be regularly performed once the diagnosis of CLD is made.

There were a few limitations of the present study, including the study being held at a single center, non-inclusion of the severity of CLD due to the unavailability of certain investigations required for determining Child-class, and inability to assess HE outcome since most patients were referred to the tertiary care level after diagnosis and laboratory investigations. Although referral of the patient may appear as a bias-causing factor, the patients were referred after they were already assessed for the outcome of the present study, i.e., presence of lower levels of either sodium or potassium levels or both, and they were kept part of the study irrespective of their referral since the data was collected before patient referral.

CONCLUSIONS

In conclusion, dyselectrolytemia is highly common in patients with cirrhotic liver disease who present with hepatic encephalopathy, with the prevalence of hypokalemia and hyponatremia in these patients being 18.9% and 38.6%, respectively. This signifies that patients presenting with this complication of liver cirrhosis should always be screened for either of these disturbances in the electrolyte levels and should be considered as a possible precipitating factor of hepatic encephalopathy, even when other obvious precipitants are clinically apparent.

Authors' Contribution

Conceptualization: TI
Methodology: TI
Formal analysis: TI
Writing and Drafting: TI
Review and Editing: TI

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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