E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.48047/ijprt/16.02.246

Research Article

Assessment of Hypokalemia Frequency and Hospital Stay Duration Among Patients with Hepatic Encephalopathy

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Abstract:

Objective: To determine the frequency and severity of hypokalemia in patients with hepatic encephalopathy and its association with the length of hospital stay.

Study Design: Hospital-based cross-sectional study.

Place and Duration: This study was carried at Jinnah Post Graduate Medical Center Karachi Pakistan from May 2025 to May 2026

Methods: A total of 150 adults with chronic liver disease or cirrhosis and diagnosed hepatic encephalopathy were enrolled through non-probability consecutive sampling. The West Haven criteria were used to grade hepatic encephalopathy. Demographic, clinical, precipitating, and treatment-related variables were recorded, and serum potassium was measured at admission prior to replacement therapy; hypokalemia was defined as a level below 3.5 mEq/L. The independent-samples t-test was used to compare the mean hospital stay between patients with and without hypokalemia, with a $p<0.05$ threshold.

Results: The mean age was 54.8 ± 11.2 years, and 96 patients (64.0%) were male. Hypokalemia was present in 53 patients (35.3%); 32 (21.3%) had mild, 15 (10.0%) moderate, and 6 (4.0%) severe hypokalemia. The mean age was significantly higher (58.9 ± 10.2 years versus 52.6 ± 11.1 years; $p=0.001$) in patients with hypokalemia than in those with normokalemia, while male sex was significantly associated with hypokalemia (75.5% versus 57.7%; $p=0.030$). The mean hospital stay was 6.7 ±

2.1 days in the hypokalemia group and 6.3 ± 1.9 days in the normokalemia group, which did not differ significantly (p=0.231).

Conclusion: Hypokalemia occurred in over one third of patients with hepatic encephalopathy and did not significantly correlate with duration of hospital stay. Regular monitoring of potassium and appropriate correction is still essential.

Keywords: *Hepatic encephalopathy; hypokalemia; frequency; hospital stay.*

Introduction

Hepatic encephalopathy (HE) is a potentially reversible but clinically serious neuropsychiatric syndrome associated with liver insufficiency and portosystemic shunting. It can range from mild attention and psychomotor deficits to disorientation, somnolence, and coma, and is often assessed by the West Haven criteria [1]. In contemporary practice, overt HE is considered a significant organic event for which prompt identification of precipitating factors is essential, since the likelihood of recurrence, functional decline, hospitalization, and death remains significant [2]. Incident HE in a population-based cohort of cirrhosis patients occurred at 11.6 cases per 100 patient-years, highlighting the high prevalence of HE in modern cirrhosis treatment [3].

The multifactorial pathophysiology of HE includes hyperammonemia, astrocyte swelling, altered brain neurotransmission, systemic inflammation, impaired cerebral energy metabolism, and gut–liver–brain axis dysfunction [4]. Hypokalemia, in particular, is an important modifiable precipitant, as potassium depletion can exacerbate ammonia neurotoxicity through several converging mechanisms. Hypokalemia induces ammoniagenesis in the kidneys, decreases urea production in the liver, and often results in metabolic alkalosis, increasing the amount of freely diffusible ammonia that can cross the blood–brain barrier [4, 5]. Experimental potassium depletion caused a 34% decrease in urea-synthesis capacity and a 7-fold increase in plasma ammonia; potassium repletion corrected these abnormalities [6]. Recent mechanistic data thus suggest that hypokalemia is not only a biochemical side effect, but also a potential active factor in HE development and progression [7].

Patients with decompensated cirrhosis may be at risk for hypokalemia due to poor oral intake, vomiting or diarrhea, secondary hyperaldosteronism, renal potassium wasting, and diuretics, such as lactulose or loop diuretics [3, 4]. However, its frequency varies across clinical settings and definitions. In a Karachi study, hypokalemia has been shown to occur in 35% of 137 HE admissions with serum potassium levels below 3.5 mEq/L [8]. One study reported hypokalemia in 78% of 5,000 patients and a progressive decrease in potassium levels in the progression of West Haven Grades [9]. A secondary-care study, however, identified hypokalemia in 18.9% of 127 patients and no significant correlation with HE grade [10].

Length of hospital stay is a clinically and economically significant outcome since an extended hospital stay could indicate delayed neurological recovery, ongoing precipitants, treatment complications, and resource utilization [11]. However, the relationship between hypokalemia and

length of stay is inconsistent. In the Karachi cohort, the mean hospital stay was 5.97 days for hypokalemic and 5.78 days for normokalemic patients, respectively, but there was no significant difference between them [8]. More recent mortality studies also show that electrolyte disturbances often occur simultaneously with severe HE, renal failure, high ammonia levels and infections, thereby introducing significant confounding potential [12].

Hypokalemia is a common, measurable and correctable abnormality. Knowledge of its occurrence and its relationship to prolonged hospitalization could help to guide earlier electrolyte monitoring and prompt potassium repletion, which may help to facilitate neurological recovery, and may decrease complications and hospital costs. Therefore, this study aims to determine the frequency of hypokalemia among patients with hepatic encephalopathy and assess its association with the duration of hospital stay.

Methodology

This hospital-based cross-sectional study population consisted of all patients with hepatic encephalopathy who were admitted to a single hospital for the first time over two years. The sample size was determined using the single-population proportion study formula, $n = Z^2p(1-p)/d^2$, with an assumed frequency of hypokalemia of 35% (as previously reported), a 95% confidence level, and an absolute precision of 8%. The sample size was determined as 150 participants. Patients were selected using a non-probability consecutive sampling technique, which involves sampling all eligible patients admitted over the study period until the required sample size was reached.

The study included patients of both sexes, aged ≥18 years, with chronic liver disease or cirrhosis who were clinically diagnosed with hepatic encephalopathy (HE). Following clinical evaluation, laboratory studies, and excluding other causes of neurological impairment, patients were diagnosed with hepatic encephalopathy if they had altered mental status and liver dysfunction or portosystemic shunting. The severity of hepatic encephalopathy was graded using the West Haven criteria. Subtle cognitive changes and sleep disturbances were defined as Grade I, lethargy, disorientation, and asterixis as Grade II, severe confusion and somnolence as Grade III, and coma as Grade IV.

Patients who had acute stroke, traumatic brain injury, central nervous system infection, epilepsy, psychiatric disorders, renal potassium wasting disease prior to admission, potassium supplementation prior to admission, or incomplete clinical records were excluded. Patients who were transferred to another facility or discharged against medical advice prior to the end of treatment were also excluded.

A structured data collection proforma was used to gather demographic and clinical data. Blood samples were drawn at admission prior to the administration of potassium replacement, and serum potassium levels were determined. Patients were divided into two groups: hypokalemic and non-hypokalemic. Patients were stratified into those with hypokalemia (serum potassium < 3.5 mEq/L) and those

without hypokalemia. Hospital stay was derived as the number of days between admission and discharge or in-hospital mortality.

The data were analyzed statistically using SPSS software. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The percentage of hypokalemia was defined as the percentage of patients with a potassium level below 3.5 mEq/L. Mean hospital stay was compared between patients with and without hypokalemia using an independent t-test. The test was applied after checking the assumptions of normality and homogeneity of variance. A p-value <0.05 was considered statistically significant.

Results

Among the 150 participants, the mean age was 54.8 ± 11.2 years. Most patients were male (n= 96, 64.0%), while females accounted for (n= 54, 36.0%). Urban residents were more common (n= 88, 58.7%) than rural residents (n= 62, 41.3%). Hepatitis C was the leading cause of liver disease (n= 102, 68.0%), followed by hepatitis B (n= 32, 21.3%) and alcohol-related disease (n= 16, 10.7%). Previous hepatic encephalopathy was reported in (n= 86, 57.3%). Grade II was most frequent (n= 60, 40.0%), followed by Grade III (n= 48, 32.0%), Grade I (n= 24, 16.0%), and Grade IV (n= 18, 12.0%) (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (n = 150)

Variable	Frequency (n)	Percentage (%)
Age (years), mean ± SD	54.8 ± 11.2	—
Gender		
Male	96	64.0
Female	54	36.0
Residence		
Urban	88	58.7
Rural	62	41.3
Etiology of chronic liver disease		
Hepatitis B virus infection	32	21.3
Hepatitis C virus infection	102	68.0
Alcohol-related liver disease	16	10.7
Previous history of hepatic encephalopathy		
Yes	86	57.3
No	64	42.7
West Haven grade at admission		
Grade I	24	16.0
Grade II	60	40.0
Grade III	48	32.0
Grade IV	18	12.0

Normal serum potassium levels were observed in 97 participants (64.7%), whereas hypokalemia was identified in 53 patients (35.3%). Mild hypokalemia was the most common category, affecting 32 patients (21.3%). Moderate hypokalemia was recorded in 15 patients (10.0%), while severe hypokalemia was present in 6 patients (4.0%). These findings indicate that more than one-third of the study population had potassium deficiency at admission (Table 2).

Table 2. Frequency and Severity of Hypokalemia Among Patients With HE

Serum potassium status	n (%)
Normal potassium (≥3.5 mmol/L)	97 (64.7%)
Hypokalemia (<3.5 mmol/L)	53 (35.3%)
Mild hypokalemia (3.0–3.4 mmol/L)	32 (21.3%)
Moderate hypokalemia (2.5–2.9 mmol/L)	15 (10.0%)
Severe hypokalemia (<2.5 mmol/L)	6 (4.0%)

Patients with hypokalemia were older than those without hypokalemia, with mean ages of 58.9 ± 10.2 and 52.6 ± 11.1 years, respectively, and this difference was statistically significant (p=0.001). Male patients were also more common in the hypokalemia group (n=40, 75.5%) than in the no-hypokalemia group (n=56, 57.7%), showing a significant association with gender (p=0.030). Mean serum sodium and creatinine levels did not differ significantly between groups. Infection, gastrointestinal bleeding, diuretic use, and lactulose use were more frequent among hypokalemic patients; however, none of these associations reached statistical significance (Table 3).

Table 3. Comparison of Clinical Characteristics Between Patients with and Without Hypokalemia

Variables	Hypokalemia group (n=53)	No hypokalemia group (n=97)	p-value
Age (years), mean ± SD	58.9 ± 10.2	52.6 ± 11.1	0.001
Male gender, n (%)	40 (75.5%)	56 (57.7%)	0.030
Serum sodium (mmol/L), mean ± SD	132.1 ± 4.8	133.5 ± 4.5	0.084
Serum creatinine (mg/dL), mean ± SD	1.35 ± 0.42	1.26 ± 0.39	0.201
Infection as precipitant, n (%)	18 (34.0%)	23 (23.7%)	0.178
Gastrointestinal bleeding, n (%)	12 (22.6%)	17 (17.5%)	0.448
Diuretic use, n (%)	31 (58.5%)	41 (42.3%)	0.057
Lactulose use, n (%)	44 (83.0%)	77 (79.4%)	0.590

The overall mean duration of hospital stay was 6.4 ± 2.0 days. Patients with hypokalemia had a mean hospital stay of 6.7 ± 2.1 days, whereas those without hypokalemia had a mean stay of 6.3 ± 1.9 days. The mean difference between the two groups was 0.4 days. Although patients with hypokalemia stayed slightly longer in the

hospital, this difference was not statistically significant (p=0.231). Therefore, no significant association was found between hypokalemia and duration of hospital stay among patients with hepatic encephalopathy (Table 4).

Table 4. Association Between Hypokalemia and Duration of Hospital Stay Among Patients with HE

Hospital-stay variable	Hypokalemia group (n=53)	No hypokalemia group (n=97)	Mean difference	p-value
Length of hospital stay (days), mean ± SD	6.7 ± 2.1	6.3 ± 1.9	0.4 days	0.231

Discussion

This study aimed to evaluate the frequency of hypokalemia in HE patients and its correlation with hospital duration of stay. The average age was 54.8 ± 11.2 years, and 64.0% of the subjects were males. The results are in line with those of Ullah et al., who found a mean age of 57.36 ± 17.65 years and 61.4% males [9]. Toure et al similarly showed a male predominance in 71.0% of cases, but with a lower mean age of 49.8 years [13]. Compared with this, Javed et al. reported a significantly younger age group of Pakistanis, with a mean of 36.76 years [14], and Iwasa et al. reported an older age group in a Japanese cohort, with a median age of 67 years and 53% males [15].

In the current study, hypokalemia was observed in 35.3% of patients. Two studies support the frequency. Similarly, Fahad et al. reported hypokalemia in 35% of HE patients, and there was no significant difference in stay between hypokalemic and normokalemic [8]. Javed et al. also identified hypokalemia in 63 of 179 patients (35.2%), which is very similar to our 35.3%, but they showed significantly longer hospital stays for hypokalemic patients compared to our result [14]. This contrasts with Ullah et al., who reported hypokalemia in 78% [9], and with the study in Ghana by Duah et al., which found hypokalemia in only 11.4% of patients with HE [16]. In our cohort, mild hypokalemia was most common, while moderate hypokalemia occurred in 10.0% and severe hypokalemia occurred in 4.0%. Ullah et al. also noted that most hypokalemic patients had blood levels between 2.5 and 3.4 mEg/L, confirming that although hypokalemia was common, most cases were mild to moderate [9]. This distribution is biologically consistent with the relationship between potassium and ammonia, described by Mikkelsen et al., which suggests that decreases in potassium status stimulate renal ammoniagenesis and that this process may be linked to the progressive severity of HE [6].

In this study, patients with hypokalemia were significantly older than those with non-hypokalemia. This pattern is similar to Ullah et al., where the mean age for the multinational population was 57.36 ± 17.65 years, but they primarily examined potassium in relation to HE severity [9]. On the other hand, Javed et al. did not observe any statistically significant age difference in hypokalemia (p=0.230). Their younger population may explain the disagreement

[14]. Furthermore, hypokalemia had a significant association with male sex in our study. This male predominance is similar to that observed by Ullah et al. [9] and Rudler et al. in the French intensive-care cohort (72%), but neither made sex an independent predictor [17]. In contrast, Maida et al., studying Japanese diuretics, observed hypokalemia more commonly in women, particularly in older women with renal impairment [18]. Our finding contrasts with that study, which excluded cirrhosis and HE patients, so the sex-related potassium risk is not independent of disease, renal function, or drug exposure.

Hypokalemia was associated with increased, though not statistically significant, rates of infection, gastrointestinal bleeding, and the use of diuretics or lactulose. Poudyal et al. reported infections (49.2%), electrolyte disturbances (41.0%), and gastrointestinal bleeding (16.0%) in HE admissions [19]. Rudler et al. described infection in 64%, bleeding in 36%, hyponatremia in 22% and several precipitants in 82% of intensive-care patients [17]. Likewise, Dutta et al. noted that the most common precipitants were lactulose failure, infection, and gastrointestinal bleeding [20]. These studies support the clinical importance of these factors, but none was significantly associated with potassium status in our results.

The hospital stay was only 0.4 days longer with hypokalemia in this study, indicating no significant association. This is in contrast to the significantly longer duration of hypokalemia-related hospitalization reported by Javed et al. [14]. In the study by Poudyal et al., the duration of stay was reported as 7.0–9.64 days based on treatment regimen [19]. This association between hospitalization duration and variceal bleeding, chronic kidney disease, and MELD score has been suggested by Zhang et al., who concluded that length of stay was multifactorial [21].

The clinical implications of these results are that potassium should be measured at admission and during hospital stays, particularly in elderly patients, diuretic therapy, and patients with gastrointestinal losses. Potassium correction is still essential, although it was not statistically related to stay; hypokalemia can increase ammonia production and neurological dysfunction. Electrolyte replacement should thus be provided along with systematic evaluation and treatment of infection, gastrointestinal bleeding, renal dysfunction, dehydration, constipation, and precipitants due to medication use in inpatient HE care [20, 21].

This single-center cross-sectional study had a relatively small sample size and could not establish a causal relationship between hypokalemia and hospital stay. Liver disease severity and treatment-related variables were not comprehensively adjusted.

Conclusion

In this study, hypokalemia was observed in over one-third of the patients with hepatic encephalopathy. Hypokalemia was significantly associated with older age and male sex. Hypokalemic patients had a mean hospital stay slightly longer than that of the normokalemic patients, but the difference was not significant. The results

emphasize the need for routine potassium monitoring and prompt correction in patients with hepatic encephalopathy. Larger multicenter prospective studies are needed to determine if hypokalemia is a disease-specific predictor of severity, hospitalization, readmission, mortality, and clinical outcomes.

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