ORIGINAL ARTICLE

IMPACT OF HYPOKALEMIA ON HEPATIC ENCEPHALOPATHY AND ITS EFFECT ON DURATION OF STAY IN HOSPITAL

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Background: Hypokalemia is one of the most important precipitating factors of hepatic encephalopathy causing Hypokalemic Alkalosis which is the leading cause of increased levels of nonionic ammonia in blood that crosses the blood brain barrier with ease and accumulates in the Central Nervous System. **Methods:** A descriptive study was conducted in the Department of Medicine, PAF Hospital, Islamabad from December 31, 2022, to January 1, 2024.The sample size was calculated using WHO sample size calculator and non-probability sampling technique was used. Calculation of mean and standard deviation for variables like Age, Potassium levels and Length of Hospital Stay was done. Frequencies and percentages were calculated for variables like Hypokalemia, Gender, and Ethnicity. Independent samples t-test was used to compare the means, duration of stay at the hospital for patients with and without hypokalemia, keeping the *p*-value $\leq$0.05 as significant. **Results:** The mean age of patients was 36.76±9.52 years. Out of the total 179 patients considered, 109 patients were male while 70 were females. Sixty-three patients were found to have hypokalemia. Their mean Potassium level was 3.47±0.37 mEq/L. A significant difference (*p*=0.230) wasn't detected in patients presenting with hypokalemia with age greater than and less than 35 years of age whereas, a significant difference (<0.001) was detected in the age group of less than 35 years when mean length of hospital stay was calculated. **Conclusion:** The mean length of hospital stay was significantly higher amongst patients having hypokalemia, compared to those with no hypokalemia.

Keywords: Hepatic Encephalopathy; Hypokalemia; Liver Cirrhosis; Alkalosis

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INTRODUCTION

The World Health Organization (WHO) defines cirrhosis as the conversion of normal liver parenchyma into structurally abnormal nodules accompanied with fibrosis.[1] Cirrhosis is one of the most common causes of mortality in our society with viral hepatitis (B & C) being its most important etiological factor. 70% of all the patients diagnosed with cirrhosis[2] also have Hepatic Encephalopathy (HE) which would later on become the cause of death in 30% of them.[3] There is 26% probability in a patient suffering from cirrhosis for five years to develop an episode of Hepatic Encephalopathy.[4] The prognosis is very poor after the first episode of Hepatic Encephalopathy with survival rate for five year being only 16–22% as compared to that of 55–70% in patients suffering from cirrhosis without any evidence of HE.[4] Some of these patients may have chronic neuropsychiatric symptoms because of Porto systemic shunting of blood (Porto Systemic Encephalopathy, PSE) while other patients may develop an acute episode due to a precipitating event of Hepatic Encephalopathy. The Porto systemic encephalopathy group commonly presents with changes in personality and there is gradual intellectual deterioration. These patients tend to have relatively better survival when compared to those patients in whom Hepatic Encephalopathy is precipitated by some acute event (100% vs 70-80%).[5] The duration of stay at hospital of patients with acute Hepatic Encephalopathy is between 5 to 7 days.[6] The duration of hospital stay is considerably longer amongst patients with hypokalemia (*p*-value=0.001), with prevalence of low serum potassium level in Hepatic Encephalopathy secondary to cirrhosis of 35%.[7]

In 80% of the cases presenting with Hepatic Encephalopathy, the precipitating factors can be identified. Treatment of the precipitating event is the hallmark of treatment of patients having episode of HE. One of the most important precipitating factors is Hypokalemia.[3] There is increased levels of nonionic ammonia in patients with Hypokalemic alkalosis. This readily crosses the blood brain barrier to get concentrated in the central nervous system. Large amounts of ammonia can be detected in basal ganglia and cerebellum of cirrhotic patients with acute episode of Hepatic Encephalopathy.

The study highlights that patients with Hepatic Encephalopathy due to hypokalemia have

increased morbidity as compared to Hepatic Encephalopathy patients who have normal potassium level.

MATERIAL AND METHODS

This is a descriptive study was conducted in Department of Medicine, PAF Hospital, Islamabad, during December 31, 2023, to January 1, 2024. WHO samples size calculator was used to calculate the sample size, keeping the confidence interval at 95%. Non – probability consecutive sampling technique was deployed. The approval of ethical committee of PAF Hospital, Islamabad was sought prior to the commencement of study and informed consent was taken. A structured Performa was made, and data collection was done by using checklist.

West Haven Classification grades were used for diagnosis of HE on basis of clinical examination. Potassium levels <3.5 mEq/L by hospital lab were used to make the diagnosis of hypokalemia in these patients. Baseline demographic data collected for both the groups included age, gender, and ethnicity. The Outcome assessed was the length of hospital stay. All patients regardless of gender in the age group 12 to 60 years having acute cirrhotic encephalopathy were included while patients diagnosed with acute fulminant hepatitis, stroke, non-cirrhotic portal hypertension, uremia, Hypoglycemic and Hyperglycemic coma were excluded.

Data analysis was performed using SPSS V 21.0 for windows. The mean and standard deviation was calculated for quantitative variable like age, potassium levels and length of hospital stay and for qualitative variables like hypokalemia, gender and ethnicity, frequencies and percentages were calculated. Mean duration of stay at hospital was compared between patients with and without hypokalemia by independent samples t-test with p value of ≤0.05 being considered as significant.

Variables affecting results like age, gender & ethnicity were addressed by stratification. After stratification chi-square test was applied for hypokalemia & t-test was applied for mean duration of stay at hospital, in both the groups.

RESULTS

The mean age of patients was 36.76±9.52 years. Out of the total 179 patients included in the study, 109 (60.9%) patients were male while 70 (39.10%) were females. 121 (67.60%) patients had the age of less than or equal to 35 years while 58 (32.40%) had the age of more than 35 years as shown in Figure 1.

Out of the total 179 patients 63 (35.20%) patients were found to have Hypokalemia. The mean Potassium levels was 3.47±0.37 mEq/L with a maximum level of 3.9 mEq/L and a minimum level of 2.6 meq/L.

Table 1 shows comparison of hypokalemia with respect to age. 39 (32.2%) patients less than or equal to 35 years presented with Hypokalemia while 24 (41.4%) patients with age more than 35 years presented with Hypokalemia. There was no significant difference (p=0.230) detected when comparison was made with respect to hypokalemia.

Table 2 shows the mean duration of stay at hospital in patients with and without hypokalemia. In patients with age less than or equal to 35 years, the mean hospital stay with hypokalemia is around 6.87 days while of those with hypokalemia is around 6.16 days. A significant difference (p<0.001) can be seen in this age group whereas, in patients more than 35 years, the mean hospital stay with hypokalemia is around 6.83 days while the mean hospital stay without hypokalemia is around 6.62 days. No significant difference (p<0.393) can be seen in this age group.

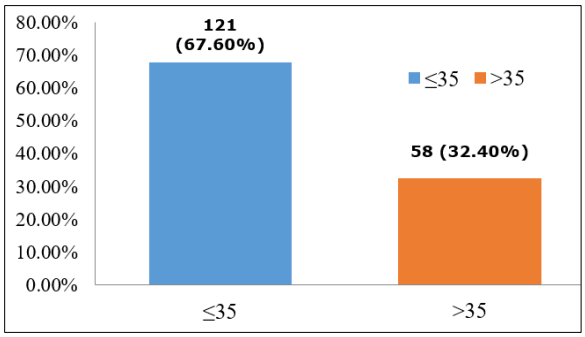

Figure-1: Age of Patients

Table 1: Comparison of hypokalemia with respect to age

Age (in years)	Hypokalemia		Total	*p*-value
	Yes	No		
≤35	39 (32.2)	82 (67.8)	121 (100)	0.230
>35	24 (41.4)	34 (58.6)	58 (100)	
Total	63 (35.2)	116 (64.8)	179 (100)	

Table-2: Mean duration of Stay in hospital in patients with and without hypokalemia

Age (in years)	Mean Hospital Stay with Hypokalemia		*p*-value
	Yes	No	
≤35	6.87±0.92	6.16±0.90	<0.001
>35	6.83±0.96	6.62±0.92	0.393

DISCUSSION

Almost 30–45% of the patients suffering from cirrhosis are prone to developing hepatic encephalopathy, same goes for patients with trans jugular intrahepatic Porto systemic shunt but their range is slightly wide, beginning from 10% and peaking up to 50%. Meanwhile, 20–60% of patients

with hepatic disease have bright chances of developing minimal hepatic encephalopathy. All these statistics suggest that HE is the most common complication of liver cirrhosis.[8]

Etiology has a great influence over the epidemiological distribution of liver cirrhosis which is quite evident by the geographical difference as well. Although alcoholism is of common practice in the West, chronic Hepatitis C infection has also been the main contributing factor to the development of cirrhosis. Meanwhile, the eastern hemisphere is prevalent with hepatitis infection, which is also the leading etiology of cirrhosis in that region.[9]

In Asia, the mainland is prevalent with Hepatitis B virus infection,[10] yet majority of the Japanese suffering from cirrhosis are infected with hepatitis C virus (HCV).[11]

In Southeast Asia, toxicity with aflatoxins and parasitic infections[12] have been involved in developing cirrhosis, while in Australia, hemochromatosis has played a great role[13]. In patients with Diabetes Mellitus that are obese as well, Nonalcoholic steatohepatitis (NASH) have emerged as the primary cause of encephalopathy. The variations in the cause of cirrhosis are markedly high when considering the incidence of hepatocellular and cholangiocarcinoma. However, currently there is no information available whether the cause of liver cirrhosis affects the development of HE.[9]

The potassium levels are usually normal in patients suffering from liver disease, although both hyperkalemia and hypokalemia can occur. Aldosterone secretion is increased in these patients leading to potassium and sodium secretion but decreased distal sodium delivery counteracts for that effect of aldosterone resulting in potassium retention in the body.

The causes of hypokalemia in these patients include low potassium intake or shifting of extracellular potassium to intracellular space under the influence of alkalemia.[14] Other reasons of hypokalemia in these patients include potassium loss with the use of diuretics, hyperaldosteronism, vomiting or magnesium depletion in alcoholic cirrhosis.[15] Often, many factors are involved in causing hypokalemia. In early studies low levels of potassium were demonstrated in 30–40% of the patients regardless of the stage of the liver disease.[15,16]

Hepatic encephalopathy is worsened by hypokalemia as it increases renal ammonia genesis resulting in high systemic ammonia levels.[17] Treatment with Chlorothiazide has been associated with deterioration of hepatic encephalopathy due to hypokalemia as described by Read *at al*[17]. Studies later on also revealed that a good number of patients on diuretics developed hypokalemia due to marked renal potassium wasting.[18,19]

In 1966 another study revealed a spike in blood ammonia levels with induction of hypokalemia correlated [20]. In this study, hypokalemia was found in 63 (35.2%) patients. Mean length of hospital stay was significantly higher amongst patients with hypokalemia as compared to the patients with no hypokalemia (6.86±0.93 vs. 6.29±0.93, *p*-value <0.001).

Hypokalemia typically causes muscle weakness, ileus, polyuria, polydipsia, and myocardial irritability. Patients receiving Terlipressin for the treatment of variceal bleed showed exacerbation of hypokalemia.[21]

CONCLUSION

The frequency of hypokalemia was found in 35.2% of patients with HE secondary to cirrhosis. Furthermore, the mean length of hospital stay was significantly higher amongst patients with hypokalemia as compared to those with no hypokalemia.

AUTHORS' CONTRIBUTION

Add the contribution of each author.

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