



## ASSOCIATION OF SPONTANEOUS HEPATIC ENCEPHALOPATHY IN HIGH PROTEIN DIET CONSUMER PATIENTS OF CHRONIC LIVER DISEASE.

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### ABSTRACT

**OBJECTIVE:** To determine the association of spontaneous hepatic encephalopathy in high protein diet consumer patients of chronic liver disease CLD. **STUDY SETTING:** This descriptive study was carried out at gastroenterology department of Asian Institute of Medical Sciences Sindh Pakistan. **STUDY DURATION:** Six months from April 2019 to October 2019. **METHODS:** All the individuals admitted in the gastroenterology department with hepatic encephalopathy, of any gender who were 18 years of age or older were included. After taking complete medical history and clinical examination, patients were evaluated regarding rich protein diet consumption to observe the high protein diet consumption as a critical element in the development of hepatic encephalopathy. The information was gathered exclusively through a study proforma, and data analysis was conducted using SPSS version 26. **RESULTS:** A total of 92 patients of hepatic encephalopathy with average age of 54.36±11.3 years with male predominance were studied. Hepatitis C was the commonest etiological factors of the chronic liver disease. High-protein diet exhibited a reduced occurrence of hepatic encephalopathy, with rates of 3.3% for grade-I, 7.6% for grade-II, 4.3% for grade-III, and 4.3% for the grade-IV, in contrast to the usual diet group. Fewer patients in the high protein diet group experienced infection 3.3% compared to the usual diet group 34.8% p-0.050. Furthermore, the high protein diet group showed the significantly lower rate of AKI 1.1% compared to the usual diet group 23.9%, p-0.034. **CONCLUSION:** Hepatic encephalopathy and other complications were highly prevalent in low protein diet compared to the rich protein diet. It was observed that the rich best nutritional diet is decrease the disease prognosis compared to the formal diet.

**KEY WORDS:** CLD, encephalopathy, rich protein diet.

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### INTRODUCTION

Chronic liver disease CLD and acute hepatic failure can lead to a prevalent and consequential condition referred to as hepatic encephalopathy.<sup>1</sup> The wide spectrum of neuropsychiatric abnormalities, encompassing subtle changes in cognitive function minimal cognitive deficits as well as more pronounced symptoms such as confusion, dizziness, and loss of consciousness, represents the neuropsychiatric manifestations of hepatic encephalopathy. The clinical and financial burdens associated with hepatic encephalopathy HE are substantial, leading to a marked rise in morbidity and mortality rates, while also leading to poor quality of life.<sup>1</sup> CLD is a huge problem that affects people all over the world.<sup>2</sup> Alcohol consumption is the main causative factor of CLD in the western countries, whereas hepatitis B virus and C virus are seeming to be the main causes in Pakistan.<sup>2</sup> HE is occurring in up to 70% among all cirrhotic patients, such as cases

having abnormalities that can only be demonstrated by psychological tests.<sup>2,3</sup> Of those suffering from chronic liver disease, approximately 30% of the cases pass away as a result of hepatic encephalopathy.<sup>2,4</sup> There seems to be the number of conditions that can lead the HE, including infections, constipation, bleeding in the GITs, vomiting/diarrhea, hypoglycemia and the hypoxia. There are two components involved in the management of hepatic encephalopathy: the first is to eliminate the precipitating cause as much as possible, as well as 2nd is to prevent the causative factors.<sup>5</sup> On the other hand, malnutrition is also an approximation for hepatic encephalopathy, are among the commonest consequences of cirrhosis, and have a negative impact on the prognosis.<sup>6,7</sup> Because muscle tissue plays a significant role in the elimination of circulatory ammonia, the decrease of skeletal mass may further complicate

neuropsychiatric state.<sup>6,8</sup> Therefore, enhancing nutritional quality instance, by changing the accessibility of substrates, making use of specific substrates, or manipulating metabolic regulatory, possibly help avoid the HE development and make its management easier when it is already present.<sup>6</sup> Although there is a rate of poor nutrition in the cases having cirrhosis is 61%, and it often worsens as the disease develops.<sup>9</sup> There is growing scepticism over the efficacy of severe and extended protein restrictions as a therapeutic for hepatic encephalopathy as a result of a worsening in the patient's nutritional state and the metabolic disturbances that are linked with it.<sup>9</sup> On the other hand, according to a comprehensive review, the case series studies containing limited numbers of individuals demonstrated that a vegetarian protein intake minimizes the manifestations of HE compared to the meat based diet.<sup>10</sup> However this study has been done to determine the association of spontaneous hepatic encephalopathy in high protein diet consumer patients of chronic liver disease.

#### MATERIAL AND METHODS

This descriptive study was conducted at gastroenterology department of Asian Institute of Medical Sciences Sindh Pakistan, during six months of duration from April 2019 to October 2019. All the individuals admitted in the gastroenterology department with hepatic encephalopathy, aged 18 years or older, regardless of gender, were eligible for inclusion criteria. All the patients of multiorgan failure, patients with pre-existing cognitive impairment or neurological conditions unrelated to hepatic encephalopathy, patients currently participating in other clinical trials, patients with severe comorbidities specifically severe heart disease or uncontrolled diabetes and those participants who declined to take part in the study were not included.

**Table 1.** Descriptive statistics of age, gender and etiological factors in patients with CLD n=92

Variables		Descriptive statistics	
Age mean		54.36±11.14 years	
Gender	Male	61	66.3
	Female	31	33.7
	Total	92	100.0
Etiological factors	HCV	62	67.4
	HBV	9	9.8
	C2H5OH	10	10.9
	HBV+HDV	4	4.3
	HBV+HCV	5	5.4
	NBNC	2	2.2
	Total	92	100.0

**Table 2.** SHE and other complications in accordance to high protein diet consumer patients of CLD n=92

Variables	DIET		p-values
	Usual diet	High protein diet	
Grades of encephalopathy	Grade - I	1314.1%	33.3%
	Grade - II	2729.3%	77.6%
	Grade - III	2729.3%	44.3%
	Grade - IV	77.6%	44.3%
Precipitant	Infection	3234.8%	33.3%
	Electrolyte imbalance	1617.4%	22.2%
	UGIB	33.3%	11.1%
	Constipation	11.1%	11.1%
	None	1920.7%	1112.0%

Participants were informed about the study's objectives and purpose, and verbal consent was obtained. Each patient underwent a thorough medical history assessment and clinical examination by qualified healthcare professionals. The primary focus of the evaluation was to identify the consumption of a high protein diet as a potential key factor in the pathogenesis of hepatic encephalopathy. Data collection was carried out using a structured study proforma designed to capture relevant information. Subsequently, all collected data was meticulously recorded and organized. SPSS version 26 was used for the data analysis.

#### RESULTS

The average age of the study subjects was found to be 54.36±11.14 years. In terms of gender distribution, 66.3% of the patients were male, while 33.7% were female. Regarding etiological factors, the study found that 67.4% of the patients had Hepatitis C HCV, followed by 9.8% with Hepatitis B, 10.9% with alcohol consumption, 4.3% cases had both HBV and Hepatitis D, 5.4% had both HBV and HCV, and 2.2% had non-viral, non-alcoholic causes.

**Table 1.** The results showed that in the high protein diet group, a lower percentage of patients experienced HE, grade I was in 3.3% cases, grade II was in 7.6% patients, grade III was in 4.3% and 4.3% cases had grade IV, compared to the usual diet group. P-value 0.411 suggest no significant difference. When looking at precipitating factors, fewer patients in the high protein diet group experienced infection 3.3% compared to the usual diet group 34.8%. There was a statistically significant difference observed, as indicated by a p-value of 0.050. In terms of complications, the high protein diet group had a significantly lower incidence of AKI 1.1% compared to the usual diet group 23.9%, p- 0.034. **Table 2**

<b>AKI</b>	Yes	2223.9%	11.1%	0.034
	No	5256.5%	1718.5%	
<b>HCC</b>	Yes	2122.8%	33.3%	0.310
	No	5357.6%	1516.3%	

## DISCUSSION

Hepatic encephalopathy stands as the commonest complication in instances of advanced liver disease.<sup>11,12</sup> HE represents a distinct form of cerebral dysfunction frequently associated with liver cirrhosis, featuring a range of nonspecific neurological and psychiatric.<sup>11,13</sup> symptoms. In individuals afflicted with liver disease, the state of their diet and nutritional well-being plays a crucial role as both a therapeutic intervention and a prognostic determinant.<sup>14</sup> In this study, we have explored the intricate relationship between spontaneous hepatic encephalopathy HE and dietary habits, specifically focusing on the consumption of high protein diets, in patients diagnosed with chronic liver disease CLD. In this study the mean age of the patients was 54.36 years, 66.3% were male and 33.7% were female. Consistently Mumtaz SU et al<sup>15</sup> reported that the average age of the patients was 54.23 years, with 54 54% being male and 46 46% being female. On the other hand Qazi A et al<sup>16</sup> also found consisting findings as the mean age was 48.12  $\pm$ 8.521 years, and the gender distribution consisted of 61.54% males and 38.46% females. The observed male dominance in the CLD having hepatic encephalopathy HE could be recognized to numerous factors, but it's essential to note that this is not a universal phenomenon. Certain forms of viral hepatitis, such as hepatitis B and C, are most common among males, which can increase the likelihood of CLD and HE in this population. Although the hormonal differences between men and women can also influence liver metabolism and response to liver injury. Estrogen, for example, is thought to have protective effects on the liver.

In this study, the etiological factors contributing to hepatitis were analyzed, revealing that Hepatitis C HCV was the most prevalent factor, followed by 9.8% with Hepatitis B, 10.9% with alcohol consumption, 4.3% cases had both HBV and Hepatitis D, 5.4% had both HBV and HCV, and 2.2% had non-viral, non-alcoholic causes. These findings are consistent with previous research conducted by the Qazi A et al<sup>16</sup>, Tauseef A et al<sup>17</sup> and Shah Zeb MA et al<sup>18</sup>.

In this study it has been revealed that in the high protein diet group, a lower percentage of patients experienced HE, with 3.3% in "Grade-I, 7.6% in Grade-II, 4.3% in Grade-III, and 4.3% in Grade-IV", paralleled to the formal diet group P-0.411, infection was lower 3.3% in contrasted to the formal diet group 34.8% and in terms of complications, the high protein diet group had a significantly lower incidence of AKI and HCC compared to the usual diet group p- <0.05. On the other hand, it is reported that, since the late 1800s, it has been demonstrated that reducing protein intake can be beneficial for hepatic encephalopathy. Recent clinical research indicates that a significant portion of individuals with cirrhosis may be able to handle a regular

amount of protein in their diet.<sup>19</sup> Nevertheless, roughly one-third of cirrhotic patients experiencing hepatic encephalopathy are unable to tolerate a normal level of protein intake.<sup>19</sup> Our findings were supported by Kroupina K et al<sup>20</sup>, sustained consumption of elevated levels of protein over an extended period did not preserve muscle mass or reduce ammonia levels. However, it did result in a decrease in oxidative stress, which in turn contributed to the prevention of hepatic encephalopathy HE. This was evidenced by improvements in both short- and long-term memory, reduction in anxiety, and enhanced locomotor activity. It was also demonstrated that providing a sudden increase in protein intake was safe for cirrhotic rodents, as it did not lead to an elevation in ammonia levels or trigger the onset of hepatic encephalopathy.<sup>20</sup> Furthermore Iqbal U et al<sup>21</sup> reported that contemporary evidence has shifted the previously held belief regarding protein restriction in cirrhosis patients. Nowadays, it is advisable to offer a daily protein intake within the range of 1.2 to 1.5 grams per kilogram of body weight. This study findings suggest several significant trends in the high protein diet group compared to the usual diet group. However, it's essential to acknowledge a key limitation in this study, which is the relatively small sample size of only 18 patients in the high protein diet group. With a limited number of participants, the study may not adequately capture the variability within the high protein diet group. Individual variations in response to dietary interventions could be missed. To strengthen the validity and generalizability of these findings, further research with a larger and more diverse patient population is needed. Additionally, conducting randomized controlled trials can help mitigate some of the limitations associated with small sample sizes and provide more robust evidence for the effects of a high protein diet on hepatic encephalopathy, infection rates, and complications like acute kidney injury AKI.

## CONCLUSION

In conclusion, our study examined the impact of a high protein diet on patients with Chronic Liver Disease CLD in relation to hepatic encephalopathy HE, precipitating factors, and acute kidney injury AKI. The results indicated that in the high protein diet group had rate of HE, infections, AKI and HCC compared to the group following a usual diet. These findings suggest that a high protein diet may have a beneficial impact on reducing infection risk and AKI in CLD patients. However, the influence of diet on HE and HCC development may be more complex and require further investigation.

**ETHICS APPROVAL:** The ERC gave ethical review approval.

**CONSENT TO PARTICIPATE:** written and verbal consent was taken from subjects and next of kin.

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**CONFLICT OF INTEREST:** No competing interest declared.

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