Factors Influencing the Outcome in Hepatic Encephalopathy Patients: Preventable Factors Worsen the Outcome

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Abstract

Objective: To determine the factors that influence the outcome in terms of death or survival in patients who presented with hepatic encephalopathy in our tertiary care hospital.

Material and Methods: This was a prospective observational study[13] performed at Department of Medicine, Hepatology and Gastroen-terology, SIMS, Lahore, from June 2022 to May 2023. After written informed consents, patients who presented with hepatic encephalopathy were enrolled. Their demographic features and laboratory indices were noted. These patients were followed for the outcome in terms of death (group A) or no death (group B) during hospitalization. SPSS-27 was used for analysis. Independent sample T test and Chi-square test were used to compare two groups with quantitative and quantitative variables respectively. The p-values were labelled significant if <0.05. The regression analysis was also executed to find the likelihood of worse outcome.

Results: Amongst 325 hepatic encephalopathy patients, 80.3% recovered while 19.7% died during hospitalization. Age (p=0.924), weight (p=0.123), initial MELD score (p=0.943) and initial platelet count (p=0.977) were comparable in both groups. The occurrence of death had no significant association with gender (p=0.481), etiology of cirrhosis (p=0.592), HRS (p=0.592), and comorbidities (p=0.252). The death occurred 26.3 times more in patients who aspirated, 63.4 times more in who had no history of endoscopy, and 24.9 times more in who presented with upper GI bleed.

Conclusion: The inpatient mortality was significantly high in hepatic encephalopathy patients who got pulmonary aspiration, who presented with upper GI bleed, and who had no history of endoscopy. Age, gender, MELD score, etiology of cirrhosis, hepatorenal syndrome, and comorbidities did not significantly take part in the mortality of these patients.

Keywords: Liver cirrhosis, Hepatic encephalopathy, outcome, mortality.

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Introduction

Hepatic encephalopathy is a serious neurological complication of liver dysfunction.[1] It occurs in upto 40% of the patients with liver cirrhosis.[2] Hyperammonemia is thought the culprit neurotoxin, however exact pathogenesis is unknown.[3-5] Infection[6] and upper GI bleed[7] are the commonest precipitants leading to recurrent episodes of hepatic encephalopathy resulting repeated hospitalizations. Correction of precipitating factors usually reverses the encephalopathy; however, sometimes outcome is fatal.[8] Once hepatic encephalopathy has occurred, median survival of cirrhotic patients is foreshortened to one to two years.[9] A lot of work on precipitating factors of hepatic encephalopathy is available nationally and internationally.[10-12] However, knowledge about the factors contributing the mortality in patients with hepatic encephalopathy is scarce in our working setups. If some reversible factors are there,

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then the outcome of these patients can be improved. This made the author keen to pick this subject as his research protcol. Hence, the objective of our study was to determine the factors that influence the outcome in terms of death or survival in patients who presented with hepatic encephalopathy in our tertiary care hospital.

Material and Method

This was a prospective observational study[13] performed at Department of Medicine, Hepatology and Gastroenterology, SIMS, Lahore, from June 2022 to May 2023. After ERC permission and written informed consents, 325 patients of age 12 years and above, from both genders who presented with hepatic encephalopathy were enrolled. Their demographic features and laboratory indices were noted. History was taken regarding etiology of cirrhosis, upper GI endoscopic procedure, and comorbidities, while examination was performed for the presence of pulmonary aspiration and upper GI bleed at presentation. Investigation data for MELD score, hepatorenal syndrome and platelet count was also collected at presentation. These patients were followed for the outcome in terms of death or discharge from the hospital. SPSS-27 was applied for analysis process, and the all enrolled patients were grouped into two batches: hepatic encephalopathy patients who died (Group A) and hepa-tic encephalopathy patients who did not die (Group B). Independent sample T testing was done to collate studied batches with quantitative variables including age, weight, MELD score and platelet count. While Chi-square testing was done to collate two batches with qualitative variables including gender, etiology of cirrhosis, pulmonary aspiration, history of upper GI endoscopy, upper GI bleed, HRS, and comorbidities. The p-values were labelled significant if <0.05. Regression was executed was applied to find out the impact of different prognosticators on the likelihood that the death would be the end-result of the hospitalized patients with hepatic encephalopathy.

Results

Amongst 325 hepatic encephalopathy patients, 19.7% (n=64) died during hospitalization while 80.3% (n=261) recovered from hepatic encephalopathy. Age (p=0.924), weight (p=0.123), MELD score at the time of hospitalization (p=0.943) and initial platelet count (p=0.977) were comparable in patients who died and who did not die during hospitalization **(Table 1)**.

Bivariate analysis showed that death was significantly

Table 1: *Comparison of quantitative variables with outcome of hepatic encephalopathy patients (n = 325) **

	Qualitative variables	Outcome of the patients		Mean difference	p-value
		Death (n=64)	No-death (n=261)		
1.	Age (years)	54.33 ± 18.99	54.07 ± 19.99	0.26	0.924
2.	Weight (kg)	65.58 ± 17.38	68.92 ± 15.03	3.35	0.123
3.	MELD score at presentation	19.23 ± 6.48	19.16 ± 7.60	0.07	0.943
4.	Platelet count ($x10^3$ /ml)	101.17 ± 56.79	101.34 ± 37.83	0.17	0.977

**Independent sample T-test was used*

Table 2: *Comparison of qualitative variables with outcome of hepatic encephalopathy patients (n = 325) **

Quantitative variables	Outcome of the patients		p-value	Odd Ratio with 95% CI
	Death (n=64)	No-death (n=261)		
Sex:				
Male	34 (53.1%)	153 (58.6%)	0.481	1.250(0.7
Female	30 (46.9%)	108 (41.4%)		22-2.165)
Etiology of cirrhosis:				
Viral	58 (90.6%)	243 (93.1%)	0.592	0.716(0.2
Non-viral	06 (9.4%)	18 (6.9%)		72-1.884)
Pulmonary aspiration:				
Yes	48 (75.0%)	04 (1.5%)	<0.01	192.750
No	16 (25.0%)	57 (98.5%)		(61.758-601.583)
Index or follow -up upper GI endoscopy:				
Yes	04 (6.3%)	246 (94.3%)	<0.01	0.004(0.0
No	60 (93.7%)	15 (5.7%)		01-0.013)
Upper GI bleed at presentation:				
Yes	54 (84.4%)	09 (3.4%)	<0.01	151.2(58.
No	10 (15.6%)	252 (96.6%)		634-389.901)
HRS at presentation:				
Yes	06 (9.4%)	18 (6.9%)	0.592	1.397(0.5
No	58 (90.6%)	243 (93.1%)		31-3.674)
Comorbidities:				
Yes	09 (14.1%)	24 (9.2%)	0.252	1.616(0.7
No	55 (85.9%)	237 (90.8%)		11-3.670)

**Chi-square analysis was used*

Table 3: *Binary Logistic Regression to find outcome of hepatic encephalopathy patients (n=325)*

Risk Factors	B	Wald-Statistic	p-value	S.E.	Odds Ratio	95% C.I. for EXP(B)	
						Lower	Upper
Age	0.038	3.554	0.059	0.020	1.038	0.999	1.080
Sex (Male/Female)	-0.079	0.011	0.917	0.758	0.924	0.209	4.086
Pulmonary aspiration (Yes/No)	3.271	12.467	<0.01	0.926	26.335	4.286	161.830
History of Upper GI endoscopy (No/Yes)	4.149	26.330	<0.01	0.809	63.359	12.989	309.057
Upper GI bleed at presentation (Yes/No)	3.216	15.784	<0.01	0.810	24.931	5.101	121.842
Constant	-3.253	4.059	0.044	1.615	0.039		

Nagelkerke R Square = 87.4% : Cox & Snell R Square = 55.0%

higher in batch of patients suffering from hepatic encephalopathy who had pulmonary aspiration (p<0.01), no history of upper GI endoscopy (p<0.01) and who had upper GI bleed at presentation (p<0.01). However, occurrence of death amongst hepatic encephalopathy patients had no significant connection with gender (p= 0.481), etiology of cirrhosis (p=0.592), presence of HRS at presentation (p=0.592), and presence of comorbidities (p=0.252) (Table-2). Regression analysis was accomplished to ascertain the impact of sex, age, presence of pulmonary aspiration, history of upper GI endoscopy and presence of upper GI bleeding on the likelihood that death might be the outcome among hospitalized patients stricken with hepatic encephalopathy. The logistic regression replica explained 87.4% (Nagelkerke R2) of the variance in the occurrence of death among hepatic encephalopathy patients and correctly classified 97.8% of cases. Patients with pulmonary aspiration were 26.3% times likely to expire than who had no pulmonary aspiration. Similarly, hepatic encephalopathy patients who had no history of index or prior upper GI endoscopy were 63.4% times more likely to die than who had underwent upper GI endoscopy. Patients who had upper GI bleed at presentation were 24.9% times more likely to die than who had no upper GI bleeding at presentation. It was also seen that age (p=0.059) and gender (p=0.917) had no confounding effect during regression analysis (Table 3).

Discussion

The saying "prevention is better than cure" is accurately applicable in case of hepatic encephalopathy because even if patient recovers from hepatic encephalopathy, lifespan of liver cirrhosis patients is limited.[9] Well-known precipitating factors of hepatic encephalopathy include infection, upper GI bleed, electrolyte imbalance and constipation.[14] Nandu S Poudyal and colleagues[15] from Nepal observed GI bleed as precipitating factor in 16% patients with hepatic encephalopathy. Similarly, Harshal Khobragade and colleagues[16] from India mentioned upper GI bleeding in 18.6% of patients with hepatic encephalopathy. On the other hand, Anarissoh LM Lawson and his team[17] from Togo said that 33.3% hepatic encephalopathy patients had GI bleeding as precipitating factor. In our study, upper GI bleeding was seen in 19.4% patients with hepatic encephalopathy, where mortality was also significantly higher among hepatic encephalopathy patient suffering upper GI bleeding (p<0.01). On the other hand, significant number of patients (n=75, 23%) had not underwent index or prior upper GI endoscopy in our studied population. Whereas index as well as annual or biannual follow-up upper GI endoscopies for variceal detection and management are recommended in liver cirrhosis patients.[18] This drawback of our hospitalization setups put our liver cirrhosis patients at risk of overt upper GI bleed as well as obscure or occult bleeding leading to hepatic encephalopathy as well as significant risk of death due to it. In our precious study that mortality was 63.359 times higher among patients with hepatic encephalopathy who had not underwent upper GI endoscopy. This is a preventable factor, consideration of which can reduce mortality among hepatic encephalopathy patients in our country. Pulmonary aspiration is also an important issue in comatosed patients which increases morbidity and mortality of these patients.[19] The risk of aspiration increases with the grade of comma; therefore, large trials suggest the need of tracheal intubation with worsening GCS score of comatosed patients.[20] This all data is from surgical floors especially in trauma patients. Such research from gastroenterology suites esp. in hepatic encephalopathy patients are scarce. Qamar Rafiq and colleagues[21] observed pulmonary aspiration in 31.9% patients with hepatic encephalopathy. They also mentioned that patients in which hepatic encephalopathy was associated with upper GI bleeding suffered significantly more pulmonary

aspiration ($p<0.01$). In our study, we found that death was the outcome of hepatic encephalopathy episode 26.3% times more in group of patients who had pulmonary aspiration. Hence, we can say that prevention from pulmonary aspiration using maneuvers like tracheal intubation can escape a large number of hepatic encephalopathy patients from death as the outcome of hospitalization.

Conclusion

The inpatient mortality was significantly high in hepatic encephalopathy patients who got pulmonary aspiration, who presented with upper GI bleed, and who had no history of upper GI endoscopy procedure. Age, gender, MELD score, etiology of cirrhosis, hepatorenal syndrome, and comorbidities did not significantly take part in the mortality of these patients. Prevention from aspiration using maneuvers like tracheal intubation, applying index and follow-up upper GI endoscopies in cirrhotic patients for variceal screening and management can effectively reduce the mortality by hepatic encephalopathy in our population.

Conflict of Interest *None*

Funding Source *None*

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Authors Contribution

MI, IAK: Conceptualization of Project
MI, IAK, TR: Data Collection
AM, AN: Literature Search
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IAK, AMC: Drafting, Revision
MI, TR: Writing of Manuscript