

PREDICTORS OF OUTCOME IN PATIENTS WITH TYPE C HEPATIC ENCEPHALOPATHY

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ABSTRACT

Background: Hepatic encephalopathy is a spectrum of neuropsychiatric manifestations observed in patients with hepatocellular dysfunction. We conducted this study to determine the outcome of patients with type C hepatic encephalopathy. **Methods:** This descriptive study was conducted in Gastroenterology Unit, PGMI Hayatabad Medical Complex Peshawar from January 2009 to June 2010. A total of 316 patients presenting with type C hepatic encephalopathy were included. Those with type A and B encephalopathy and toxic/metabolic encephalopathy were excluded. Patients were graded according to West-Haven criteria (I-IV). Precipitating cause was determined from history, examination and relevant investigations. Outcome was defined in terms of morbidity and mortality. All patients received the standard treatment. **Results:** Out of 316 cirrhotics, 167(52.8%) were males and 149(47.2%) females with mean age 53±12.4years. Constipation was the most common precipitating factor for encephalopathy occurring in 231(78.1%) patients, followed by esophageal variceal bleed and infection in 47(14.8%) and 38(12.1%) patients respectively. Out of these, 276(87.3%) had West-Haven stage I-III and 40(12.7%) stage IV encephalopathy. Mean duration of hospital stay was 5±2 days in patients with West-Haven stage IV and 4±2 days in West-Haven stage I-III. The overall mortality was 8(2.5%) with West-haven stage I-III encephalopathy and 39(97.5%) with stage IV encephalopathy and esophageal variceal bleed with hemoglobin less than 5gm/dl ($p < 0.003$). **Conclusion:** West-Haven stage IV and esophageal variceal bleed as the precipitating cause in type C hepatic encephalopathy is associated with high morbidity and mortality.

KEY WORDS: Cirrhosis, Hepatic encephalopathy, Hepatic encephalopathy grade C, Variceal bleed.

INTRODUCTION

Hepatic encephalopathy (HE) is a spectrum of neuropsychiatric manifestations observed in patients with hepatocellular dysfunction when other causes of encephalopathy such as toxic, metabolic or intracranial lesions have been excluded.¹ The exact pathophysiology of hepatic encephalopathy is unknown but evidence so far has clearly shown it to be multifactorial.² The most widely accepted theory implicates a myriad of gut-derived toxins in the pathogenesis of HE, the prototype of which is ammonia.³ Phenols, thiols, and short-chain fatty acids are the other putative gut-derived toxins.⁴ Modulation of gamma-aminobutyric acid (GABA) and endogenous benzodiazepines (BZPs) systems resulting in widespread inhibition of the cerebral cortex through their corresponding receptor-mediated altered neurotransmission have also been proposed as possible mechanisms.⁵ Previously the terms acute and chronic hepatic encephalopathy were used in the setting of acute liver failure and cirrhosis liver respectively which lacked standardization and resulted in a lot of confusion. In 2002, a working committee task force on hepatic encephalopathy standardized the definition and classified HE into

Types A, B and C on the basis of the disease state.⁶ Type C hepatic encephalopathy, associated with cirrhosis and portal hypertension or porto-systemic shunts was further subdivided into episodic (previously acute), persistent (previously chronic), or minimal (previously subclinical). The precipitating factors leading to hepatic encephalopathy are usually obvious and the common triggers include gastrointestinal bleeding, constipation, dehydration, infection, hypokalemia, sepsis, drug toxicity and diuretic use.⁷ Chronic liver disease and its complications like hepatic encephalopathy have significant negative impact on the psychosocial aspect of a patient's life, as evidenced by psychomotor function impairment and changes of pathologic range in personality and subjective well-being.⁸ Cirrhosis liver and its complications including hepatic encephalopathy significantly affect the health and longevity of the affected population.⁹ It has impact on the finance at individual and family level, due to direct health-care expenditures and indirect costs resulting from loss of income on part of the patient owing to premature death and /or disability.¹⁰

Hepatic encephalopathy in cirrhotic patients is one of the most common presentations to ter-

tiary care centers like ours and is associated with high morbidity and health-care resource utilization.¹¹

We conducted this study to determine the outcome of patients admitted with hepatic encephalopathy in terms of morbidity and mortality. This will help in formulating health-care policies and prioritization of health interventions.

MATERIAL AND METHODS

This study was conducted in Gastroenterology unit, Postgraduate Medical Institute Hayatabad Medical Complex Peshawar from January 2009 to June 2010.

All cirrhotic patients presenting with hepatic encephalopathy (type C) were included in the study. A total of 316 patients were recruited in the study. Cirrhosis was established on the basis of previous medical record or composite clinical, laboratory and radiological findings such as stigmata of chronic liver disease, biochemical indices including liver function tests and findings on ultrasonography of the abdomen. Patients with type A and B encephalopathy and those with other toxic/metabolic encephalopathies were excluded from the study. Type C hepatic encephalopathy was diagnosed on the basis of history, physical findings and mental status changes. Physical findings included fetor hepaticus, asterixis and focal neurological abnormalities like increased deep tendon reflexes, unilateral or bilateral upgoing plantars and other findings like ataxia, dysarthria and tremor. Mental status changes were detected by psychometric testing such as the number connection test, drawing star, spiral or square and writing name or drawing signature. Encephalopathy was graded into stages 0-4 according to West-Haven, s criteria based on level of consciousness, intellect and behaviour and neurological findings. Precipitating cause of encephalopathy was determined from detailed history and investigations like full blood count with differential, urinalysis, serum electrolytes and renal function tests.

Outcome was defined in terms of morbidity and mortality or recovery from encephalopathy and discharge from the unit. Morbidity was defined as no improvement in stage of encephalopathy or progression into a higher stage. Mortality was defined as no recovery from encephalopathy followed by death of the patient. Patients were examined daily for changes in encephalopathy stage and were followed until discharge or death. All patients received the standard regimen for treatment of hepatic encephalopathy based on non-absorbable disaccharides like lactulose and antibiotics as well as symptomatic and supportive measures.

RESULTS

A total of 316 cirrhotic patients participated in the study. Of these, 167 (52.8%) were males and 149 (47.2%) females. Mean age was 53 ± 12.4 years. Chronic hepatitis C was responsible as a cause of cirrhosis in 247 (78.1%) patients, whereas, 25 (7.9%) had chronic hepatitis B and in 44 (13.9%) patients the etiology was either unknown or uninvestigated.

Constipation was found to be the most common precipitating factor for hepatic encephalopathy occurring in 231 (73.1%) patients, followed by esophageal variceal bleed and infection which occurred in 47 (14.8%) and 38 (12.02%) patients respectively.

Out of these, 276 (87.3%) patients had West-Haven stage I-III hepatic encephalopathy and 40 (12.7%) stage IV encephalopathy at presentation.

Mean duration of hospital stay was 5 ± 2 days in patients with West-Haven stage IV encephalopathy and 4 ± 2 days in patients with stage I-III encephalopathy.

The overall mortality was 8 (2.5%) with West-haven stage I-III encephalopathy and 39 (97.5%) with stage IV encephalopathy and esophageal variceal bleed ($p < 0.003$).

DISCUSSION

Type C hepatic encephalopathy is a common complication of cirrhosis and it portends decreased survival and impaired overall quality of life.¹² The information regarding prediction of outcome in type C hepatic encephalopathy is scarce.

Various studies have shown the adverse impact of hepatic encephalopathy on survival in patients with hepatic cirrhosis.^{13,14} Sanyal et al demonstrated a strong association between MELD score and developing hepatic encephalopathy (HE) as well as HE and mortality.¹⁵ It has been postulated that hepatic encephalopathy occurs in the setting of porto-systemic venous shunting and decreased hepatocellular functional reserve which allows the various incriminated gut-derived toxins to bypass and reach the cerebral circulation and exert their noxious effects. Thus, from a pathophysiological point of view it is logical to consider that hepatic encephalopathy is an important prognostic indicator when compared with various biochemical indicators like MELD. Fichet et al studied the outcome of patients with chronic liver disease with severe hepatic encephalopathy in intensive care settings and determined that prognosis and one year mortality of intensive care unit patients with severe hepatic encephalopathy was high with arterial hypotension, mechanical

ventilation, vasopressors at any time and acute renal failure.¹⁶

Udayakumar et al studied the predictors of mortality in hepatic encephalopathy in acute and chronic liver disease and found that in patients with chronic liver disease higher grades of encephalopathy and native drug therapy, high serum bilirubin, requirement for support systems predicted a poor outcome.¹⁷ Our study also shows increased mortality with higher grades of encephalopathy and higher serum bilirubin levels which in turn increase the Child-Turcotte -Pugh score.

There is 70% chance of re-bleeding from the esophageal varices in the first bleeders and about one third of such re-bleeds prove to be invariably fatal.¹⁸ The risk of mortality is very high in the first few days after the bleed and thereafter slowly decreases over the next few weeks.

Mumtaz et al also showed in their study that higher grades of hepatic encephalopathy and the presence of two or more precipitating factors was associated with prolonged hospital stay and increased mortality.¹⁸ Similarly, Stewart et al concluded that higher grade of encephalopathy was associated with 3.9 fold increase in the risk of mortality in hospitalized patients with end stage liver disease.¹⁹ The results of our study are compatible to these.

CONCLUSION

West-Haven stage IV encephalopathy at presentation precipitated by massive esophageal variceal bleed in liver cirrhosis is associated with prolonged hospital stay and high mortality.

We recommend that patients with advanced liver disease who have episodic type C hepatic encephalopathy with the precipitating factor being esophageal variceal bleed should have intervention for obliteration of their varices by endoscopic variceal ligation or sclerotherapy to thwart the danger of future variceal bleed leading to hepatic encephalopathy which is associated with significant risk of morbidity and mortality.

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