ORIGINAL ARTICLE

Correlation Between Serum Ammonia Levels And The Severity of Hepatic Encephalopathy

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ABSTRACT

Elevated serum ammonia levels are associated with hepatic encephalopathy(HE). This study was designed to evaluate the correlation between ammonia levels and grades of HE. This study was conducted in Shalamar teaching hospital Lahore. 50 patients suffering from liver cirrhosis and presenting with altered sensorium were recruited in the study. Their serum ammonia levels, Child Pugh score, and grades of hepatic encephalopathy were determined, and correlated. Serum ammonia was normal in 18(36%) and it was high in 32(64%) patients. 15(30%) patients had grade I, 16(32%) patients had grade II, 12(24%) patients had grade III and 7(14%) patients had grade IV of hepatic encephalopathy.

Conclusion: There is positive weak correlation between ammonia levels and grades of hepatic encephalopathy. Ammonia is etiologically linked but it is not solely responsible for the increasing severity, of hepatic encephalopathy.

INTRODUCTION

Hepatic encephalopathy is one of the complications of liver cirrhosis. High circulating ammonia concentration are frequently encountered in patients with hepatic encephalopathy[1]. It is presently not known whether an additional measurement of ammonia could improve predictive accuracy in determining the risk of hepatic encephalopathy. Serum ammonia levels may be elevated in the absence of hepatic encephalopathy, therefore it is not diagnostic test. Many studies support evidence for the role of ammonia in pathogenesis of hepatic encephalopathy, and elevated levels of serum ammonia are sugesstive of diagnosis of HE, in the presence of clinical features of HE[2]. Ammonia accumulation due to decreased detoxifying capacity of liver or presence of systemic shunts, leads to neuropsychiatric manifestations of hepatic encephalopathy. These manifestations can be cognitive, psychomotor, behavioral, intellectual, emotional or fine motor functions[3]. Ammonia-induced changes occur in neurotransmitter synthesis and release, and osmotic disturbances resulting from astrocytic metabolism of ammonia to glutamine.[4] If the relationship between serum ammonia level and grades of HE is confirmed, these findings may help identifying patients as being at high risk for HE and preventive strategies may be planned to reduce the circulating ammonia concentration to interrupt disease progression.[5]

MATERIALS AND METHODS

Patients admitted in Shalamar hospital Lahore with cirrhosis and altered sensorium were recruited in study from January 2014 to October 2014.Total 50 patients of either sex were enrolled in the study. Diagnosis of cirrhosis was done by ultrasound criteria or signs of portal hypertension. Consent was taken from each patient or their attendants. Viral status of underlying liver cirrhosis was recorded, and patients suffering from both HBV and HCV associated liver cirrhosis were included in the study. Patients, undergoing hemodialysis, or having mental state changes due to other causes such as cerebro vascular disease, and uncontrolled diabetes, were excluded from study. The study was reviewed and approved by the institutional review board.

DATA COLLECTION PROCEDURES

Data was collected at the time of admission. Clinical information included age, sex, name, hospital record number, source of admission, admitting diagnosis, etiology of cirrhosis, duration of disease, Child-Pugh score at admission, prior

lactulose use, portal hypertension, dominant precipitating factor for HE, were recorded. Laboratory Data included serum albumin, total bilirubin, prothrombin time, serum ammonia level, serum creatinine, international normalization ratio (INR).Hepatic encephalopathy was diagnosed and graded as per West Haven Criteria by a single investigator of postgraduate rank at least. Diagnosis was considered established on the basis of clinical signs and symptoms, laboratory and ultrasonic evidence of liver cirrhosis, and when other causes of altered sensorium were excluded though appropriate labs. Consultant opinion on the diagnosis was taken for each patient. Serum ammonia levels were recorded and correlated according to various grades of hepatic encephalopathy in all patients. Patients later on confirmed as not having HE were excluded from the study.

RESULTS

In this study, the mean age of patients was 48.87 ± 2.34 years with 27(54%) males and 23(46%) female patients. A total of 45(90%) patients had HCV, 3(6%) patients had HBV and 2 (4%) patients had alcoholic liver disease at the time of presentation. According to Grads, 15(30%) patients had grade I, 16(32%) patients had grade II, 12(24%) patients had grade III and 7(14%) patients had grade IV of hepatic encephalopathy. In this study, 8(16%) patients had Child Pugh class A, 19(38%) patients had class B and rest of 23(46%) patients had Child Pugh class C. According to operational definition ammonia was normal in 18(36%) and it was high in 32(64%) of the patients. Out of these 32 patients with elevated ammonia levels, 9,10,9,and 4 patients suffering from grades I, II, III and IV of hepatic encephalopathy respectively, had high ammonia level with positive weak, insignificant correlation, r = 0.039 (p-value = 0.78). In Child Pugh class A, there were 5, in Child Pugh class B, there were 12 and in Child Pugh class C, there were 15 patients with higher ammonia level with weak positive insignificant correlation, r =0.023 (p-value =0.875).

Table-1: Descriptive statistics of gender and their clinical diagnosis

		Number of patients	Percentages
Gender	Male	27	54%
	Female	23	46%
Grades	**I**	15	30%
	II	16	32%
	III	12	24%
	IV	7	14%
Child Pugh Class	**A**	8	16%
	B	19	38%
	C	23	46%
Ammonia	**Normal**	18	36%
	High	32	64%

Table-2: Correlation between severities of Hepatic Encephalopathy and ammonia level

		Serum Ammonia		Spearman's Correlation
		Normal	**High**	
Grades	**I**	6(33.3%)	9(28.1%)	**r = 0.039 (p-value = 0.788)**
	II	6(33.3%)	10(31.2%)	
	III	3(16.7%)	9(28.1%)	
	IV	3(16.7%)	4(12.5%)	
Child Pugh Class	**A**	3(16.7%)	5 (15.6%)	**r =0.023 (p-value = 0.875)**
	B	7(38.9%)	12 (37.4%)	
	C	8(44.4%)	15 (46.0%)	

DISCUSSION

The etiological role of ammonia in hepatic encephalopathy was first established in 1930s[6]. The exact causal association and underlying pathophysiology is not clear, but general consensus is in favor of accumulation of gut derived toxins especially ammonia, astrocyte swelling and cerebral edema.[7] The present study was designed to evaluate the correlation between ammonia levels and grades of HE. In our study,32(64%) patients, suffering from different grades of hepatic encephalopathy had higher serum ammonia levels,and this finding is supported by already published literature[8]. Out of these 32 patients with elevated ammonia levels, 9,10,9,and 4 patients suffering from grades I, II, III and IV of hepatic encephalopathy respectively, had high ammonia level with positive weak, insignificant correlation. Our study shows that although ammonia is etiologically linked but it is not solely responsible for the increasing severity, of hepatic encephalopathy. This finding of our study is also supported in the literature.[9] In our study, it was also observed that there was overlap of values of serum ammonia levels between different grades of HE. The study reveals that there is weak positive correlation between serum ammonia level and HE grades. This observation was also made by Norenberg M. et al, who mentioned that although a high ammonia level is an independent risk factor for the development of HE, yet , the relation between the ammonia levels and severity of hepatic encephalopathy appears more complex.[10] Studies have shown decreased cerebral oxygen metabolism and blood flow in patients with cirrhosis with hepatic encephalopathy (HE). It remains unclear, whether these disturbances are associated with HE or with cirrhosis itself and how they may relate to arterial blood ammonia concentration and cerebral metabolic rate of blood ammonia.[11,12] so ,more studies need to be conducted to determine association of ammonia levels with severity of hepatic encephalopathy. If such associations are confirmed, progression to severe HE might be interrupted by taking timely remedial measures.

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