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CORRELATION OF SERUM AMMONIA LEVEL AND SERUM MAGNESIUM LEVEL WITH SEVERITY OF HEPATIC ENCEPHALOPATHY AMONG LIVER CIRRHOSIS PATIENTS

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ABSTRACT **Background:** Hepatic encephalopathy (HE) is a major neuropsychiatric complication of cirrhosis. Hyperammonemia is central to its pathogenesis, while magnesium deficiency may worsen neuronal dysfunction. **Objective:** To compare serum ammonia and magnesium levels among different grades of HE and determine their correlation with severity. **Methods:** This observational in-vivo study included 174 patients with liver cirrhosis and HE at a tertiary-care hospital over two years. HE was graded by West Haven criteria. Clinical assessment, serum ammonia, serum magnesium, hematological and biochemical investigations, and ultrasonography were performed. **Results:** Grade II HE was most frequent (36.78%). Mean Day-1 ammonia increased from 40.98±16.88 µg/dL in Grade I to 141.33±101.83 µg/dL in Grade IV ($p<0.0001$). Mean magnesium decreased from 1.76±0.24 mg/dL to 1.15±0.20 mg/dL ($p<0.0001$). Ammonia correlated positively ($r=0.441$), whereas magnesium correlated inversely ($r=-0.608$), with HE grade. **Conclusion:** Serum ammonia and magnesium may serve as useful adjunct biochemical markers for assessment and monitoring of HE severity..

KEYWORDS : Hepatic encephalopathy, liver cirrhosis, serum ammonia, serum magnesium, West Haven criteria

INTRODUCTION

Liver cirrhosis is the final stage of chronic liver injury and is characterized by diffuse fibrosis, regenerative nodules and distortion of normal hepatic architecture. Hepatic encephalopathy is among its most serious complications and ranges from subtle cognitive impairment to disorientation, stupor and coma. Overt HE is associated with recurrent hospitalization, impaired quality of life, increased healthcare utilization and poor survival.

Hyperammonemia is considered a central pathogenic mechanism. Impaired hepatic detoxification and portosystemic shunting increase circulating ammonia, which crosses the blood–brain barrier and is converted to glutamine in astrocytes. The resulting osmotic stress, astrocyte swelling, oxidative stress and mitochondrial dysfunction contribute to cerebral dysfunction. Systemic inflammation, altered neurotransmission, electrolyte abnormalities and intestinal dysbiosis act synergistically with ammonia.

Magnesium is an essential intracellular cation involved in membrane stability, neuromuscular conduction and numerous enzymatic reactions. Hypomagnesemia is common in advanced cirrhosis because of poor nutritional intake, chronic alcohol use, malabsorption, diuretic therapy, gastrointestinal losses and renal dysfunction. Reduced magnesium may enhance NMDA-receptor-mediated neuronal excitability and may aggravate neurological dysfunction. Since West Haven grading is partly subjective, objective biochemical parameters that correlate with HE severity may be clinically useful.

AIM AND OBJECTIVES

Aim: To compare serum ammonia and serum magnesium levels among different grades of hepatic encephalopathy. Objectives: (1) To grade HE using West Haven criteria; (2) to measure serum ammonia and magnesium levels; and (3) to compare these levels across HE grades and assess their correlation with severity.

MATERIALS AND METHODS

Study design and setting: An observational, in-vivo study conducted in the Department of General Medicine at a tertiary-care hospital over two years. Study population: A total of 174 adult patients diagnosed with liver cirrhosis and hepatic encephalopathy were enrolled using systematic random sampling. Patients underwent detailed history, general and systemic examination, and grading of HE according to West Haven criteria.

Investigations included complete haemogram, liver function tests, renal function tests, serum electrolytes, serum ammonia, serum magnesium and ultrasonography of the abdomen. Serum ammonia and magnesium were assessed at baseline (Day 1) and repeated on Day 5. Relevant precipitating factors, etiology, Child–Pugh class, treatment, duration of hospitalization and outcome were recorded.

Statistical analysis: Categorical variables were expressed as frequency and percentage, and continuous variables as mean±standard deviation. Chi-square test was used for categorical associations, one-way analysis of variance (ANOVA) for comparison of means across HE grades, and Pearson correlation for association of biochemical parameters with HE grade. A p value <0.05 was considered statistically significant.

RESULTS

The mean age of participants was 49.6±14.2 years and 74.71% were male. Alcohol-related liver disease was the predominant etiology (68.97%). Constipation was the commonest precipitating factor (36.21%). Child–Pugh class B was most frequent (47.13%), followed by class C (39.08%).

Table 1. Distribution according to hepatic encephalopathy grade

HE grade	Grade I	Grade II	Grade III	Grade IV	Total
n (%)	52 (29.89)	64 (36.78)	40 (22.99)	18 (10.34)	174 (100)

Interpretation: *Grade II was the commonest presentation, followed by Grade I. Most patients therefore presented with mild-to-moderate HE.*

Table 2. Association of raised serum ammonia with HE grade

Serum ammonia	Grade I	Grade II	Grade III	Grade IV
Normal, n (%)	37 (71.15)	29 (45.31)	18 (45.00)	8 (44.44)
Raised, n (%)	15 (28.85)	35 (54.69)	22 (55.00)	10 (55.56)

Interpretation: *Raised ammonia was more frequent in advanced HE grades. The association was statistically significant ($\chi^2=9.95$, $p=0.01$).*

Table 3. Serum ammonia levels according to HE severity

Time	Grade I	Grade II	Grade III	Grade IV	ANOVA ; p
Day 1, µg/dL	40.98±16.88	64.86±33.05	55.00±25.37	141.33±101.83	27.54; <0.0001
Day 5, µg/dL	36.65±16.82	59.39±32.73	46.43±15.52	121.17±51.05	31.45; <0.0001

Interpretation: *Mean ammonia was highest in Grade IV on both days. Differences across grades were highly significant, supporting a positive relationship between ammonia and HE severity.*

Table 4. Association of serum magnesium category with HE grade

Serum magnesium	Grade I	Grade II	Grade III	Grade IV
Hypomagnesemia, n (%)	20 (38.46)	30 (46.88)	31 (77.50)	18 (100)
Normomagnesemia, n (%)	31 (59.62)	34 (53.13)	9 (22.50)	0
Hypermagnesemia, n (%)	1 (1.92)	0	0	0

Interpretation: *Hypomagnesemia became progressively more prevalent with increasing HE severity and was present in all Grade IV patients (χ^2=32.13, p<0.0001).*

Table 5. Serum magnesium levels according to HE severity

Time	Grade I	Grade II	Grade III	Grade IV	ANOVA; p
Day 1, mg/dL	1.76±0.24	1.70±0.22	1.48±0.24	1.15±0.20	39.24; <0.0001
Day 5, mg/dL	1.84±0.23	1.85±0.23	1.63±0.23	1.44±0.21	21.55; <0.0001

Interpretation: *Mean magnesium declined with increasing HE grade and was lowest in Grade IV. The differences were highly significant on both Day 1 and Day 5.*

Table 6. Correlation of serum ammonia and magnesium with HE grade

Variable	Pearson r	p value	Relationship
Serum ammonia	0.441	<0.0001	Moderate positive
Serum magnesium	−0.608	<0.0001	Moderately strong inverse

Interpretation: *Worsening HE was significantly associated with higher ammonia and lower magnesium. The inverse correlation for magnesium was stronger than the positive correlation for ammonia.*

The duration of hospital stay increased from 6.24±1.83 days in Grade I to 17.83±2.18 days in Grade IV. Overall, 165 patients (94.83%) were discharged and 9 (5.17%) died during hospitalization.

DISCUSSION

The present study demonstrated a significant relationship between serum ammonia and HE severity. Mean ammonia increased across grades and was markedly elevated in Grade IV. Pearson analysis showed a moderate positive correlation (r=0.441, p<0.0001). These observations support the established role of ammonia in astrocyte swelling, oxidative stress and cerebral dysfunction. However, ammonia alone does not fully explain HE and should be interpreted with the clinical grade, inflammatory state and other metabolic abnormalities.

A highly significant inverse relationship was observed between serum magnesium and HE severity. Hypomagnesemia increased from 38.46% in Grade I to 100% in Grade IV, and mean Day-1 magnesium decreased from 1.76±0.24 to 1.15±0.20 mg/dL. The moderately strong negative correlation (r=−0.608) suggests that lower magnesium is linked to more severe neurological dysfunction. Potential contributors include alcohol-related depletion, poor intake, diuretic use, gastrointestinal losses and advanced hepatic dysfunction.

On Day 5, ammonia levels were lower and magnesium levels improved across most grades, suggesting biochemical recovery with treatment. The progressive increase in hospital stay with HE grade further demonstrates the clinical burden of severe encephalopathy. Serum ammonia and magnesium are inexpensive and widely available, and may complement West Haven grading for severity assessment and treatment monitoring. Nevertheless, the observational design and single-centre setting limit causal inference and generalizability.

CONCLUSION

Serum ammonia levels increased significantly and serum magnesium levels decreased significantly with worsening grades of hepatic encephalopathy. Ammonia showed a significant positive correlation and magnesium a significant inverse correlation with HE severity. Both parameters may serve as useful adjunct biochemical markers for severity assessment, prognostication and monitoring of treatment response, but should be interpreted alongside clinical findings and West Haven grading. Larger multicentric studies are recommended to validate these findings and evaluate the therapeutic relevance of correcting hypomagnesemia.

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