ROLE OF PLASMA AMMONIA AS A PREDICTOR OF LIVER-RELATED MORBIDITY, HOSPITALIZATION, AND MORTALITY IN CLINICALLY STABLE CIRRHOTIC PATIENTS

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Introduction

Cirrhosis is the end-stage of chronic liver injury, characterized by fibrosis and regenerative nodules, most commonly caused by viral hepatitis, alcohol abuse, metabolic dysfunction, autoimmune, biliary, and genetic disorders.(1) Ammonia is a gut-derived neurotoxin central to hepatic encephalopathy (HE), with a clear link to cerebral edema in acute liver failure, but its role in cirrhosis-related HE is less defined and remains controversial in routine practice. It also contributes to complications like liver cell injury, immune dysfunction, sarcopenia, and portal hypertension.(2)

Aim of the Work

The aim of the current study was to test the hypothesis that level of hyperammonemia is a predictive factor for liver-related complications and mortality in clinically stable cirrhotic patients.

Patients and Methods

This prospective, observational cohort study enrolled 100 adult patients aged over 18 years with established cirrhosis, confirmed by clinical features and characteristic ultrasonographic findings, from the Hepatobiliary Unit, Alexandria University Hospitals. Both compensated and decompensated but clinically stable patients were included, provided they had no acute decompensation, major bleeding, or any event requires hospital admission in the past 30 days, and no chronic kidney disease, malignancy, hematological disorders, prior organ transplant, or inherited hyperammonemia. All patients underwent clinical and laboratory assessments, including CBC, liver and renal function tests, serum electrolytes, AFP, and coagulation profile.

Severity was determined by Child-Turcotte-Pugh (CTP) and MELD-Na scores. Plasma ammonia was measured for all patients at the start of the study. Abdominal ultrasonography was performed to assess liver morphology, splenic size, and ascites.

Upper endoscopy was used to evaluate varices and portal hypertensive gastropathy. Patients were prospectively followed for up to 12 months. Endpoints were liver-related hospitalization, transplantation, death, or study closure.

Results

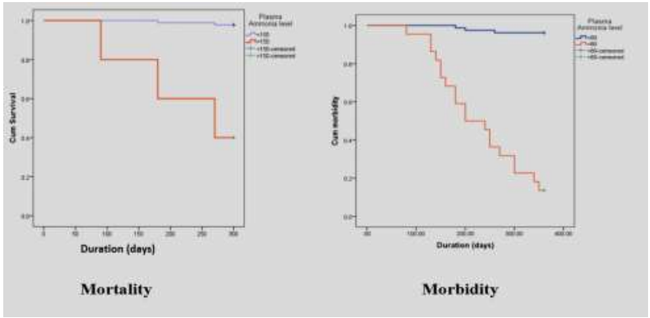
Table 1: Shows the baseline data of the study population

	Result (Total No=100)
Age (Mean±SD)	55.38±6.9
Gender	
Male	59
Female	41
Etiology of liver disease	
AIH	1
HBV	11
HCV	80
MASLD	2
Unknown	6
Clinical jaundice	5
Clinical ascites (mild)	22
History of GIT bleeding	14
Type of GIT bleeding	
H&M	10 (71.4%)
Melena	4 (28.6%)
Platelets (Mean±SD)	112.07±31.96
Potassium (Mean±SD)	3.81±0.22
Child Pugh score (Mean±SD)	5.81±0.77
MELD-NA (Mean±SD)	10.37±4.16
Plasma Ammonia (Mean±SD)	71.77±36.45

During the follow up period, 22 patients required hospitalization due to liver related complications including 3 cases of spontaneous bacterial peritonitis, one case of cholangitis, 15 cases of variceal bleeding, 3 cases with over hepatic encephalopathy and 13 cases of new onset or worsening of ascites. Death occurred in 8 patients.

The ROC analysis showed that plasma ammonia at a cut-off value of 150.0 µmol/L could predict mortality with a sensitivity of 95.0% and a specificity of 90.0%, with an AUC of 0.949 and a p-value of 0.0001. Additionally, a cut-off value of 80.0 µmol/L could predict morbidity (hospitalization) with a sensitivity of 98.0% and specificity of 93.0%, with an AUC of 0.984 and a p-value of <0.0001.

Cox regression analysis identified elevated plasma ammonia, higher Child-Pugh and MELD-Na scores, and lower platelet counts as the only significant predictors of morbidity ($p < 0.05$). Additionally, elevated plasma ammonia, increased INR and bilirubin levels, decreased platelet counts, and lower potassium levels were the significant predictors of mortality ($p < 0.05$).



Kaplan-Meier curves for mortality and morbidity

Conclusion

Elevated plasma ammonia levels in clinically stable cirrhotic patients are strong predictive markers for liver-related morbidity, hospitalization, and mortality. Cut-off values of 80 µmol/L for morbidity and 150 µmol/L for mortality showed high sensitivity and specificity, indicating plasma ammonia's valuable role in risk stratification.

Monitoring plasma ammonia can aid early identification of high-risk patients, guiding timely interventions to improve prognosis in cirrhosis.

References

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