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CORRELATION OF OPTIC NERVE SHEATH DIAMETER WITH SERUM AMMONIA LEVELS IN ACUTE ON CHRONIC LIVER FAILURE AND DECOMPENSATED CHRONIC LIVER DISEASE

Clinical Science

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ABSTRACT

Background: Acute on Chronic Liver Failure (ACLF) and decompensated Chronic Liver Disease (CLD) are associated with hepatic encephalopathy (HE) and potential cerebral edema due to hyperammonemia. Optic Nerve Sheath Diameter (ONSD) measurement is a non-invasive tool for assessing intracranial pressure (ICP), but its correlation with serum ammonia levels remains unclear. **Aims:** This study aimed to evaluate the association between ONSD and serum ammonia in patients with ACLF/CLD and HE, assess the prevalence of cerebral edema, and determine ONSD's predictive role in outcomes. **Methods:** A prospective cohort study was conducted on intubated patients with HE (grades III/IV). ONSD was measured via ultrasound 3 mm behind the globe. Serum ammonia levels were monitored daily. Clinical outcomes, including mortality and HE severity, were analyzed. **Results:** Median serum ammonia was 105 µmol/L (IQR: 80–150), with higher levels in HE patients (p=0.067). No significant correlation was found between ONSD and ammonia (p=0.34). ONSD did not differ significantly across HE grades, Child-Pugh scores, or survival status. **Conclusion:** While elevated ammonia levels were observed in ACLF/CLD patients with HE, ONSD did not correlate strongly with ammonia or predict outcomes. ONSD remains a feasible, non-invasive tool for ICP assessment, but larger studies are needed to define its clinical utility in liver failure-related cerebral edema.

KEYWORDS

Optic Nerve Sheath Diameter, serum ammonia, hepatic encephalopathy, cerebral edema, liver failure.

INTRODUCTION

Acute on Chronic Liver Failure (ACLF) is a potentially reversible condition in patients with Chronic Liver Disease (CLD) with or without cirrhosis that is associated with the potential for multiple organ failure and mortality within 3 months in the absence of treatment of the underlying liver disease, liver support, or liver transplantation.[7]

Decompensated Chronic Liver Failure is defined as an acute deterioration in liver function in a patient with cirrhosis and is characterised by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal haemorrhage.[1]

Cerebral edema is hypothesized to occur as a result of ammonia accumulating in glial cells, which is then converted to glutamine, resulting in an osmotic gradient and cellular edema.[2,3] Vasodilatation and cerebral hyperperfusion may also play a role.[2,3] Monitoring of Intra Cranial Pressure (ICP) may permit therapeutic intervention before cerebral herniation and devastating brain injury occurs.

An enlarged Optic Nerve Sheath Diameter (ONSD) may reflect elevated intracranial pressure (ICP) being transmitted to the perineural subarachnoid space.[8,9] An increased ONSD may reflect an early increase in intracranial pressure.

Ammonia is a by-product of nitrogen metabolism, and its formation in the body is predominantly a consequence of the action of the enzyme glutaminase located within enterocytes of the small intestine and colon, as well as the action of the vast number of urease-producing bacteria located in the gut. Ammonia derived from the gut is absorbed into the hepatic portal circulation and transported to the liver where, under normal physiological conditions, it enters the urea cycle and is metabolized. Ammonia that bypasses this primary fate is subsequently 'picked up' and detoxified by glutamine synthetase (GS), an enzyme found in the hepatocytes surrounding the hepatic vein (as well as in muscle and astroglial cells), which catalyses the conversion of ammonia and glutamate to glutamine.[10]

Insult to the liver, whether acute or chronic in nature, reduces its capacity to metabolize ammonia and this exerts an ammonia burden on extrahepatic tissues which can result in hyperammonaemia up to five times that of normal blood ammonia levels.

High ammonia concentrations are closely related to a high incidence of cerebral edema and herniation.[6]

Patients with Hepatic Encephalopathy (HE) can have cerebral oedema and increased intracranial pressure. Patient with Acute Liver Failure (ALF) have cerebral edema whereas prevalence of cerebral edema in patients of CLD/ACLF with HE is not clearly reported.

In this study, we aim to determine prevalence of cerebral edema in patients of CLD and ACLF with HE by using ONSD and its association with serum ammonia level.

The lack of information between the correlation of ONSD and serum ammonia serves a warrant to undertake this prospective cohort study.

AIMS AND OBJECTIVES

Primary

- To assess the prevalence of Cerebral edema in patients of CLD/ACLF.
- To evaluate the association of ONSD with serum ammonia in patients of chronic liver disease or Acute on chronic liver failure with hepatic encephalopathy.

Secondary

- To assess whether ONSD can be used as a tool to predict outcome in patients with hepatic encephalopathy.
- To assess whether ONSD correlates with Non Contrast CT (NCCT) head findings.
- To assess whether ONSD can correlate with the severity of liver disease.

Inclusion Criteria:

Age 14- 70[25] years of age
Patients with ACLF (as defined by APASL[26])
Patients with Chronic Liver Disease (Proven histopathologically, clinically or radiologically)
Hepatic encephalopathy grade III/IV
Endotracheally intubated and mechanically ventilated

Exclusion Criteria:
Patient's relatives not willing to give consent.
Patients with already raised intracranial pressure due to infarcts (Ischemic/haemorrhagic), SOL's, Traumatic Brain Injury, etc.

METHODOLOGY

Approval of the Institutional Ethical Committee (IEC) of Mahatma Gandhi Medical College and Hospital, Jaipur, was obtained before the start of the study. Written, informed consent was taken from the guardians of the patients. This was a Prospective Study of one year duration, conducted in the Department of Critical Care Medicine and Department of Hepatology, Mahatma Gandhi Medical College and Hospital, Jaipur.

We enrolled patients with chronic liver failure with hepatic encephalopathy grade III/IV who were endotracheally intubated on mechanical ventilation. All routine baseline investigations (including Haemogram, liver function test, renal function test and coagulation profile) were sent. A baseline Serum Arterial ammonia was done. Fundoscopy and NCCT Head were also done at the time of admission.

Baseline ONSD estimation was done. Patient was kept in supine position, keeping head in midline with 30° elevated from horizon. Thick layer of ultrasound gel was applied on the closed eyelid. 10 MHz linear array probe was used for ONSD estimation. ONSD was measured 3 mm behind the globe in each eye. For each eye, three readings were taken at a time and average of the three readings was noted as final ONSD for that eye at that time. The average of right and left eye was taken as the ONSD value for final analysis. A mean binocular ONSD > 4.6 mm in female and 4.8 mm in male was considered abnormal. The patients were started on treatment as per the Standard Protocol. ONSD and arterial ammonia was measured every 24 hours, until the patient improved, ie, improvement in hepatic encephalopathy, weaned and extubated from ventilator or followed for 5 days or until mortality.

Sonosite (Ultrasonography) Machine used for the measurement of ONSD

ONSD measurement take 3mm behind the globe.

50 Patients of ACLF/CLD in Hepatic Encephalopathy grade III/IV on Mechanical Ventilation.

- ºRoutine blood investigations (CBC, LFT, KFT, Coagulation Profile)
- ºSerum Arterial Ammonia at baseline
- ºFundoscopy
- ºNCCT Head

ONSD at baseline

- Anti Hepatic Encephalopathy measures as per Standard Medical Protocol

ONSD and arterial ammonia every 24 hours

Intent Intervention:
Technique of ammonia estimation –
Anti Hepatic Encephalopathy measures as per Standard Medical Protocol

- midline head with elevation by 30 degrees and minimal stimulation.
- laxatives (lactulose),
- topical antibiotics (rifaximin),
- Hypertonic saline infusion targeting a serum sodium level between 145–155 mEq/L,
- Propofol infusion (1-5 mg/kg/h), &
- continuous renal replacement therapy (CRRT)

RESULTS

	All cases (n = 74)	Survive (n = 56)	Non survive (n = 18)	*P* value
ONSD (mm) mean±SD	5.27±0.82	5.30±0.87	5.21±0.65	0.708
Child Pugh Score; Class A+B n (%)	33 (45)	29 (88)	4 (12)	0.028
Child Pugh Score; Class C n (%)	41 (55)	27 (66)	14 (34)	
HE; Grade 1+2 n (%)	50 (68)	41 (82)	9 (18)	0.067
HE; Grade 3+4 n (%)	24 (32)	15 (63)	9 (38)	
Ammonia (ng/dL) mean±SD	247±103	260±102	208±98	0.062
Glucose (mg/dL) mean±SD	146±61	147±64	143±50	0.790
Creatinine (mg/dL) mean±SD	1.5±1.0	1.4±1.0	1.8±1.0	0.69
Sodium (mmol/L) mean±SD	134±5	135±5	131±6	0.19
Potassium (mmol/L) mean±SD	4.4±0.8	4.3±0.6	4.8±1.1	0.008
Lactate (mmol/L) mean±SD	3.3±3.3	2.9±2.7	5.0±4.4	0.050
sGPT (IU/L) mean±SD	55±84	40±63	100±129	0.008
sGOT (IU/L) mean±SD	91±140	75±96	144±223	0.066
Albumin (g/dL) mean±SD	2.9±0.6	3.0±0.6	2.7±0.7	0.182
pH mean±SD	7.4±0.1	7.5±0.1	7.3±0.2	0.106
HCO_3 mean±SD	21.3±4.3	22.7±2.8	18.8±5.9	0.005
INR mean±SD	1.5±0.4	1.5±0.3	1.7±0.5	0.024

HE: hepatic encephalopathy, ONSD: optic nerve sheath diameter, SD: Standart deviation, sGOT: Serum glutamic oxaloacetic transaminase; sGPT: Serum glutamic pyruvic transaminase; INR: International normalized ratio.

The median value of venous ammonia was 105 micromol/L (80-150 micromol/L). Higher levels of ammonia were seen in HE group as compared to the non HE group, p value 0.067. On subgroup analysis in patients with high ammonia levels (> 152 micromol/L), no significant difference was found.

Table 3: ONSD Measurements

ONSD measurements	Case group mean±SD (min-max)	Control group mean±SD (min-max)	*P* value
Average ONSD*	5.27±0.82 (3.8–8.3)	4.73±0.57 (3.5–6.2)	<0.001
Right ONSD	5.29±0.79 (3.8–8.3)	4.76±0.56 (3.2–6.1)	<0.001
Left ONSD	5.26±0.93 (3.6–9.2)	4.70±0.64 (3.0–6.3)	<0.001

*Average ONSD = The mean of right and left ONSD measurements
ONSD: optic nerve sheath diameter, SD: Standart deviation

Table 4: ONSD Measurement According To Mortality, HE And Child Pugh

		n (%)	ONSD-*mm* mean±SD (min-max)	*P* value
Mortality	Survive	56 (76)	5.30±0.87 (3.8–8.3)	0.708
	Non-Survive	18 (24)	5.21±0.65 (3.9–6.5)	
HE	Grade 1	13 (18)	4.97±0.69 (3.8–6.3)	0.348
	Grade 2	37 (50)	5.40±0.95 (3.9–8.3)	
	Grade 3	18 (24)	5.17±0.63 (4.0–6.1)	
	Grade 4	6 (8)	5.48±0.54 (5.0–6.5)	
Child-Pugh Score	Class A	2 (3)	5.65±0.92 (5.0–6.3)	0.505
	Class B	31 (42)	5.16±0.81(4.0–7.5)	
	Class C	41 (55)	5.35±0.83 (3.8–8.3)	

HE: hepatic encephalopathy, ONSD: optic nerve sheath diameter

There was no difference between the ONSD of the patients in the different grades of HE group and in different classification as per the Child Pugh system. There was no significant difference between ammonia levels and ONSD measurement (p 0.34).

DISCUSSION

In our study, we found high levels of ammonia in patients with acute on chronic liver failure (ACLF); however, the result was not statistically significant. However, other studies have shown controversial results.

Various studies have tried to understand the effects of raised serum ammonia levels and understand its correlation in liver diseases.

Ammonia was first implicated in the pathogenesis of HE by a team of Nobel Prize winning physiologists led by Pavlov and Nencki at the Imperial Institute of Experimental Medicine in Russia in the 1890's.

The inability of the bypassed liver to convert the neurotoxic ammonia into urea and its subsequent accumulation in the brain, in the syndrome which was later termed HE.[12,13]

Bernal and colleagues demonstrated ammonia to be an independent risk factor for the development of both HE and ICH, with the latter occurring in 55% of patients with blood ammonia concentrations >200 μmol/L.[11] Blood ammonia levels ≥150 μmol/L have also been shown to predict a greater likelihood of cerebral herniation and death in patients presenting with ALF.[14] Persistent arterial hyperammonaemia for 3 days following hospital admission predicts a greater likelihood of complications and death in individuals with ALF.[15]

Halimar et al. included 498 patients with liver cirrhosis and showed that the serum ammonia level is highly correlated with the severity of HE and the incidence of 28 deaths in patients with liver cirrhosis[16].

A review of the literature indicated that elevated serum ammonia contributes to neurotoxicity, sarcopenia, and immune dysfunction in cirrhosis. However, serum ammonia testing has not had consistent benefit in clinical diagnosis or management of HE in cirrhosis.

A retrospective study by Haj et al[17] found that when serum ammonia levels were obtained, this did not influence practitioner use of lactulose or overall management of HE. Furthermore, ammonia levels were not associated with time to improvement in HE. Gonzalez and Tapper[18] assessed practitioner response to serum ammonia levels obtained in cirrhosis and found that the posttest probability of HE was the same as the practitioner's pretest probability, indicating low test utility. For those with high probability of HE, the level did not change the diagnosis, whereas for those with low probability of for HE, it led to overuse of lactulose.

An ammonia level ≥ 89 μmol/L was associated with a higher frequency of organ failure (cerebral 36.2% versus 5.2% ($P < 0.001$); coagulation 39.7% versus 16.4% ($P < 0.001$)). In addition, an ammonia level ≥ 89 μmol/L was associated with severe ACLF in a study done by Chenxia Hu et al[19]

Noninvasive Intracranial Pressure Assessment by ONSD measurement by ultrasound in patients with ALF has been investigated in 3 studies[20,21,22] Using a prospective cohort of 22 pediatric patients with ALF (30-day survival rate of 45.5% and LT rate of 81.8%), Helmke et al.[20] reported an association of higher ONSD with lower survival. In another prospective cohort of 41 pediatric patients with ALF (undefined survival rate of 41.5% and LT rate of 0%), Das et al.[21] also reported an association of higher ONSD with lower survival.

Filipe S. Cardoso et al study[23] showed that the correlation between ammonia and ONSD was poor (Pearson's $r = 0.11$). Das et al.[24] reported a higher but still modest correlation between ammonia and ONSD ($r = 0.42$).

The absence of adverse effects related to ONSD measurement by ultrasound reinforces it as an easy to learn (learning curve of ≤10 procedures), widely available (transducer in regular ultrasound machine), not time-consuming (≤10 min per patient), and safe technique to perform at the bedside.[20,21,22]

A study by Chiriac et al (27) has shown that high ammonia levels are associated with severe HE and that ammonia levels can be used as a predictive tool for in hospital patients with ACLF. However, the role of ammonia level assessment and it's role in predicting HE and mortality in patients with ACLF, is still controversial.

Ammonia levels are considered unspecific for HE severity and is not used to influence management protocol (17,28). Numerous conditions like gastro intestinal bleeding, acute kidney injury, infection, sepsis and systemic inflammation, aggravate the harmful effects, that ammonia has on the brain (27). Thus, even in these conditions, the patient can develop HE, even when ammonia levels are not raised.

In our study, we have also seen that ONSD values in patients with HE, increased according to the severity of HE, however, it did not reach statistical significance. There was also no significant difference in patient's Child Pugh score and ONSD measurement. There was also no significant difference in ONSD measurement between survivors and non survivors. Similar findings have been found in a study by Colak N et al (29).

The gold standard for ICP measurement is invasive ICP monitoring. However, many indirect methods of ICP estimation are available. When ICP rises, the retrobulbar segment and the aubarachnoid area are affected, which cause an increase in ONSD (29). Thus, ONSD can be measured for ICP estimation. Another study by Das et al (24), also found that ONSD measurement increase with severity of HE, but did not reach clinical significance.

ONSD measurement, being non invasive, easy to learn and perform, widely available at majority of the centres, less time consuming and with no side effects, is a safe technique to be performed at bedside. However, ijn the absence of a defined threshold for ONSD, more large prospective studies should be done, to define the cut off for ONSD measurement and also compare the efficacy of ONSD measurement with other methods of ICP estimation.

Limitations:

In our study, the single-center and study size was small to make firm conclusions about the association between ONSD and outcomes. In our study, ONSDs of survivors were higher than non-survivors. Mortality in study patients may be due to other causes (e.g. variceal bleeding, spontaneous bacterial peritonitis) rather than the severity of HE.

CONCLUSION:

This study explored the correlation between Optic Nerve Sheath Diameter (ONSD) and serum ammonia levels in patients with Acute on Chronic Liver Failure (ACLF) and decompensated Chronic Liver Disease (CLD), focusing on hepatic encephalopathy (HE). The findings revealed elevated serum ammonia levels in patients with ACLF, though the correlation with ONSD did not reach statistical significance. Similarly, ONSD measurements did not significantly differ across HE grades, Child-Pugh scores, or between survivors and non-survivors, suggesting limited predictive value for outcomes in this cohort.

Despite the lack of definitive correlation, ONSD measurement remains a promising non-invasive, bedside tool for assessing intracranial pressure, given its safety, ease of use, and accessibility. However, the absence of a standardized threshold for ONSD and the study's small sample size highlight the need for larger, multicenter prospective studies to validate these findings and establish clear clinical guidelines.

In summary, while serum ammonia levels and ONSD provide insights into the pathophysiology of HE and cerebral edema in liver failure, their clinical utility for predicting outcomes or guiding management remains uncertain. Future research should focus on refining these biomarkers and integrating them with other diagnostic modalities to improve patient care in this high-risk population.

REFERENCES

1. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology. 2013;144(7):1426-37.
2. Raghavan M, Marik PE. Therapy of intracranial hypertension in patients with fulminant hepatic failure. Neurocrit Care. 2006;4(2):179-89.
3. Vaquero J, Chung C, Blei AT. Brain edema in acute liver failure. A window to the pathogenesis of hepatic encephalopathy. Ann Hepatol. 2003;2(1):12-22.
4. Mattos ÂZ, Mattos AA. Letter to the Editor: Acute-on-Chronic Liver Failure: Conceptual Divergences. Hepatology. 2019;70(3):1076.
5. Sundaram V, Jalan R, Wu T, et al. Factors Associated with Survival of Patients With Severe Acute-On-Chronic Liver Failure Before and After Liver Transplantation. Gastroenterology. 2019;156(5):1381-91.e3.
6. Clemmesen JO, Larsen FS, Kondrup J, Hansen BA, Ott P. Cerebral herniation in patients with acute liver failure is correlated with arterial ammonia concentration. Hepatology. 1999;29(3):648-53.
7. Bajaj JS, Moreau R, Kamath PS, et al. Acute-on-chronic liver failure: Getting ready for prime-time. Hepatology. 2018;68(4):1621-32.
8. Hansen HC, Helmke K. The subarachnoid space surrounding the optic nerves. An

ultrasound study of the optic nerve sheath. Surg Radiol Anat. 1996;18(4):323-8.
9. Hansen HC, Helmke K. Validation of the optic nerve sheath response to changing cerebrospinal fluid pressure: ultrasound findings during intrathecal infusion tests. J Neurosurg. 1997;87(1):34-40.
10. Liaw SH, Kuo I, Eisenberg D. Discovery of the ammonium substrate site on glutamine synthetase, a third cation binding site. Protein Sci. 1995;4(11):2358-65.
11. Bernal W, Hall C, Karvellas C, et al. Arterial ammonia and clinical risk factors for encephalopathy and intracranial hypertension in acute liver failure. Hepatology. 2007;46(6):1844-52.
12. Nencki M, Pawlow J, Zaleski J. Ueber den ammoniakgehalt des blutes under der organe und die harnstoffbildung bei den saugethieren. Arch Fuer Exp Pathol Pharmakol. 1896;37:26-51.
13. Shawcross DL, Olde Damink SWM, Butterworth RF, Jalan R. Ammonia and hepatic encephalopathy: the more things change, the more they remain the same. Metab Brain Dis. 2005;20(3):169-79.
14. Clemmesen J, Larsen F, Kondrup J, Hansen B, Ott P. Cerebral herniation in patients with acute liver failure is correlated with arterial ammonia concentration. Hepatology. 1999;29:648-53.
15. Kumar R, Shalimar, Sharma H. Persistent hyperammonemia is associated with complications and poor outcomes in patients with acute liver failure. Clin Gastroenterol Hepatol. 2012;10(8):925-31.
16. Shalimar, Sheikh MF, Mookerjee RP, et al. Prognostic role of ammonia in patients with cirrhosis. Hepatology. 2019;70(3):982-94.
17. Haj M, Rockey D. Ammonia Levels Do Not Guide Clinical Management of Patients With Hepatic Encephalopathy Caused by Cirrhosis. Am J Gastroenterol. 2020;115(5):723-8.
18. Gonzalez JJ, Tapper EB. A Prospective, Blinded Assessment of Ammonia Testing Demonstrates Low Utility Among Front-Line Clinicians. Clin Gastroenterol Hepatol. 2021;19(3):593-5.e1.
19. Hu C, Huang K, Zhao L, et al. Serum ammonia is a strong prognostic factor for patients with acute-on-chronic liver failure. Sci Rep. 2020;10(1):16970.
20. Helmke K, Burdelski M, Hansen HC. Detection and monitoring of intracranial pressure dysregulation in liver failure by ultrasound. Transplantation. 2000;70(2):392-5.
21. Das MC, Srivastava A, Yadav RK, Yachha SK, Poddar U. Optic nerve sheath diameter in children with acute liver failure: A prospective observational pilot study. Liver Int. 2020;40(2):428-36.
22. Rajajee V, Williamson CA, Fontana RJ, Courey AJ, Patil PG. Noninvasive Intracranial Pressure Assessment in Acute Liver Failure. Neurocrit Care. 2018;29(2):280-90.
23. Cardoso FS, Pereira R, Moreno R, Karvellas CJ, Germano N. Optic Nerve Sheath Diameter in Acute Liver Failure: A Prospective Cohort Study. GE Port J Gastroenterol. 2021;28(3):170-8.
24. Das MC, Srivastava A, Yadav RK, Yachha SK, Poddar U. Optic nerve sheath diameter in children with acute liver failure: A prospective observational pilot study. Liver Int. 2020;40(2):428-36.
25. Scahill RI, Frost C, Jenkins R, Whitwell JL, Rossor MN, Fox NC. A longitudinal study of brain volume changes in normal aging using serial registered magnetic resonance imaging. Arch Neurol. 2003;60(7):989-94.
26. Sarin SK, Kedarisetty CK, Abbas Z, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL) 2014. Hepatol Int. 2014;8(4):453-71.
27. Chiriac S, Stanciu C, Cojocariu C, et al. Role of ammonia in predicting the outcome of patients with acute-on-chronic liver failure. World J Clin Cases. 2021;9(3):552-64.
28. Ong JP, Aggarwal A, Krieger D, et al. Correlation Between Ammonia Levels and the Severity of Hepatic Encephalopathy. Nutr Clin Pract. 2003;18(4):413-4.
29. Colak N, Bayrak Basakci O, Bayram B, et al. Optic nerve sheath diameter in patients with hepatic encephalopathy. PLoS One. 2022;17(11):e0277643.