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Serum ammonia levels and bioavailability of vitamin D in patients of alcohol dependence and its role in prediction of alcoholic liver disease

Abstract

Background: Alcohol dependence is a psychiatric diagnosis. The individual drinking alcohol is dependent either physically or psychologically. Nitrogen metabolism produces ammonia. In liver it is converted to urea. Multiple enzymatic reactions are involved. Alcoholic liver disease can be detected by this parameter. Vitamin D is a fat-soluble vitamin and the study aimed to measure its levels in alcohol dependence. **Objective:** The present study was conducted to study the serum ammonia levels and bioavailability of vitamin D in patients with alcohol dependence and its role in the prediction of alcoholic liver disease. **Methods:** The study was conducted on 100 alcohol dependence patients from the psychiatric department and was allocated into two groups- group A (alcohol dependence patients with liver disease) and group B (alcohol dependence patients without liver disease). For qualitative data, chi-square test was used. Quantitative data were analysed using student t-test. A p-value of 0.05 is considered to be insignificant. The data compiled were analysed with GraphPadInStat® 3 statistical software. **Results:** Demographic variables (age, sex, weight in kg) were comparable between the two groups with the p-value remaining insignificant when comparison was done between the two groups. The average ammonia levels of Group A (87.76 μ/dl) and Group B (25.68 μ/dl) was significant when compared. The average vitamin D levels of Group A (43.58 ng/mL) and Group B (44.92 ng/mL) was non-significant when compared. **Conclusion:** As per the study results obtained, we concluded that serum ammonia levels were in a higher range than normal in the group of patients with liver disease and normal range in the group without liver disease and no significant difference was seen between the two groups concerning serum vitamin D levels.

Keywords: Psychiatric diagnosis, Nitrogen metabolism, Fat-soluble vitamin.

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INTRODUCTION

Previously in the psychiatric diagnosis of alcohol dependence, the individual drinking alcohol is dependent upon it either physically or psychologically. In 2013 it was reclassified as alcohol use disorder (alcoholism) along with alcohol abuse in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorder (DSM-5).[1] According to the fourth edition (DSM-IV) criteria for alcohol dependence, at least three out of seven of the following criteria must be manifest during a 12-month period: [2]

1. "Tolerance
2. Withdrawal symptoms or clinically defined alcohol withdrawal syndrome
3. Use in larger amounts or for longer periods than intended
4. Persistent desire or unsuccessful efforts to cut down on alcohol use
5. Time is spent obtaining alcohol or recovering from the effects
6. Social, occupational, and recreational pursuits are given up or reduced because of alcohol use
7. Use is continued despite knowledge of alcohol-related harm (physical or psychological)"

Various metabolic mechanisms are involved in eliminating alcohol form the body. Aldehyde dehydrogenase (ALDH), alcohol dehydrogenase (ADH), cytochrome P450 (CYP2E1), and catalase are the primary enzymes involved. Alcohol consumption, alcohol-related tissue damage, and alcohol dependence are influenced by variations in the genes for these enzymes. Oxygen deficits (i.e., hypoxia) in the liver is caused by alcohol metabolism. Alcohol metabolism byproducts interact with other cell components. Harmful

compounds (i.e., adducts) are thus formed. In addition, highly reactive oxygen-containing molecules (i.e., reactive oxygen species [ROS]) are also formed. These can damage other cell components. The ratio of nicotine adenine dinucleotide hydride (NADH) to NAD^+ (i.e., the cell's redox state) is changed. Damage to tissue and foetus, impairment of other metabolic processes, cancer. and medication interactions are some of the end-results. Several issues related to alcohol metabolism require further research.[3]

Alcoholic liver disease

As the chief organ responsible for the breakdown of alcohol, the liver is particularly vulnerable to alcohol metabolism's effects. More than 90 percent of people who drink heavily develop fatty liver, a type of liver disease. Yet only 20 percent will go on to develop more severe alcoholic liver disease and liver cirrhosis.[4]

Nitrogen metabolism produces ammonia. In the liver, it is converted to urea. A series of enzymatic reactions is involved in the process. Liver disease and congenital or acquired defects in the urea cycle may cause elevations in the blood ammonia concentration.[5-8] Ammonia is highly neurotoxic and, along with other factors, undoubtedly contributes to the development of encephalopathy and coma which is often a terminal event in patients with severe liver disease.[5,6] Because the concentration of ammonia in hepatic portal vein blood is normally five to ten times greater than in mixed venous blood, the gastrointestinal tract is presumed to be the site of most ammonia production.[6] The liver in the hepatic portal system metabolises much of the ammonia. Our knowledge about the metabolism of ammonia is limited in the systemic circulatory system.[7-13]

Vitamin D is fat-soluble seco-steroids. Apart from increasing intestinal absorption of calcium, magnesium, and phosphate, and it too is responsible for multiple other biological effects. In humans, the most important compounds in this group are vitamin D_3 (also known as cholecalciferol) and vitamin D_2 (ergocalciferol). Cholecalciferol and ergocalciferol can be ingested from the diet and supplements. Vitamin D from the diet or skin synthesis is biologically inactive; enzymatic conversion (hydroxylation) in the liver and kidney is required for activation.[14]

Aims and objectives

a) Estimate the serum ammonia level and vitamin D in patients of alcohol dependence with and without liver disease.
b) Compare the serum ammonia level of patients with age and sex-matched control
c) Correlate the serum ammonia levels with duration of dependence, and with those having alcoholic liver disease.

MATERIALS AND METHODS

Study design

It was a case-control study. The duration of the study was one year.

Study subjects

The study subjects were divided into two groups:

Group A: Case: Alcohol dependence patients with liver disease- 50

Group B: Control: Alcohol dependence patients without liver disease- 50

Place of study

Diagnosed cases of alcohol dependence with and without liver disease were selected from the psychiatry ward, Gauhati Medical College and Hospital (GMCH), Guwahati, Assam, India. Samples were analysed in the Central Clinical Laboratory (CCL)- Biochemistry section, GMCH.

Inclusion criteria

1. Diagnosed cases of alcohol dependence with and without liver disease.
2. Age between 20 to 40 years.
3. Patient giving consent to take part in the study as well as for necessary investigation.

Exclusion criteria

1. Diagnosed cases of infectious hepatitis, hepatic carcinoma, and other malignancies and toxic hepatitis.
2. Patients taking nutritional supplements, chemotherapy, carbamazepine, valproic acid, and iron.

Sample collection

Institutional ethical clearance was taken before conducting the study. Relevant history and clinical data were noted down on a proforma. Blood samples were collected in clot vials and carried to the CCL, GMCH.

Sample analysis

The samples were analysed for ammonia and vitamin D in Vitros 5600 autoanalyser.

Statistical analysis

For qualitative data, chi-square test was used. Quantitative data were analyzed using student t-test. A p-value of 0.05 is considered to be insignificant. Statistical analysis was done with GraphPad InStat® 3 statistical software.

RESULTS

The study was conducted throughout one year duration. A total number of 100 patients was allocated into two groups of 50 each of group A and group B respectively: group A- alcohol dependence patients with liver disease and group B- alcohol dependence patients without liver disease. There were no statistical differences according to demographic data (age, sex, and weight). p-value for age (0.8375), sex (0.6820), and weight (0.6379) being nonsignificant ($p>0.05$) as seen in Table 1.

The average ammonia levels of group A (87.76 μ/dl) and group B (25.68 μ/dl) was significant when compared.

The average vitamin D levels of group A (43.58 ng/mL) and group B (44.92 ng/mL) was non-significant when compared as shown in Table 2.

DISCUSSION

Chemical levels in the blood are regulated by liver. It also excretes bile. Thus, waste products are carried away from the liver. Liver is also passed by the blood from stomach and intestines. This blood is processed and broke down and balanced by liver. As a result, nutrients are created. Drugs are metabolised into nontoxic and such forms which help body to use easily. Normally, colon and small intestine produce ammonia. It then moves to liver. Urea cycle converts to urea. Kidneys excrete urea as it is water-soluble compound. Either enzymatic defect or hepatocellular damage makes liver unable to metabolise this toxic compound. Subsequently there is rise in ammonia levels. There are other reasons too for the rise of the levels: diversion of portal blood bypassing liver to systemic circulation or infection with certain microorganisms.[15,16] Vitamin D is a fat-soluble vitamin that promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal bone mineralisation and other roles in the body, including reduction of inflammation as well as modulation of such processes as cell growth, neuromuscular and immune function, and glucose metabolism.[17] In patients with liver failure, the levels of 25-hydroxy (25-OH) vitamin D can be low due to impaired synthesis. However, liver function needs to be severely compromised for this impairment to occur. Absorption of vitamin D is caused by liver disease. Possible reason is impaired production of bile acid. Another probable condition is porta hypertension-related gut oedema.[18] Hepatic steatosis is the first stage of alcoholic liver disease. In liver cells approaching the portal tracts, there is accumulation of small fat droplets. With advancing disease, steatosis becomes marked along with hepatocellular necrosis and acute inflammation. This condition is known as alcoholic hepatitis.[19]

Table 1: Comparison of demographic parameters

Demographic parameters Mean±SD	Group A (n=50)	Group B (n=50)	p-value
Age in years	35.32±9.83	35.72±9.63	0.8375
Weight in kg	53.86±8.68	54.64±7.82	0.6379
Sex	Male=32 (64%)	Male=29 (58%)	0.6820
	Female=18 (36%)	Female=21 (42%)	
Inference	Samples were age, sex, and weight matched with p>0.05		

SD: Standard deviation

Table 2: Comparison of ammonia levels and vitamin D levels

Parameters Mean±SD	Group A	Group B	p-value
Ammonia levels µ/dl	87.76±20.43	25.68±8.13	p<0.0001
Vitamin D ng/mL	43.58±8.51	44.92±13.39	p=0.5517
Inference	Samples for ammonia levels do not match with p>0.05 but vitamin D levels matched with p>0.05		

SD: Standard deviation

The present study was undertaken in an attempt to study the serum ammonia levels and bioavailability of vitamin D in patients with alcohol dependence and its role in the prediction of alcoholic liver disease. The study was conducted in two groups- group A (alcohol dependence patients with liver disease) and group B (alcohol dependence patients without liver disease). We found that the serum ammonia levels were in a higher range than normal in the group of patients with liver disease and the normal range in the group without liver disease. On the other hand, the levels of vitamin D were normal in both groups and found non-significant when compared between the two groups. Serum ammonia however is not recommended for checking routinely in hepatic encephalopathy but normal ammonia levels in liver disease are rare[20] which can be correlated with the findings of our study. Hence serum ammonia levels can be a diagnostic parameter to detect the presence of liver disease in alcohol dependence patients. Vitamin D levels were found normal in our study in both the groups which was contradictory to studies like Ravaioli *et al.*[21] where they found lower vitamin D serum levels in patients with alcoholic liver disease and other chronic liver diseases. The reason behind the normal serum levels of vitamin D in both groups might be due to adequate sunlight exposure or adequate dietary uptake of the people of the northeast which requires further studies in this area to conclude.

Conclusion

As per the result of our study on serum ammonia levels and bioavailability of vitamin D in patients with alcohol dependence and its role in the prediction of alcoholic liver disease, we conclude that serum ammonia levels were in a higher range than normal in the group of patients with liver disease and normal range in the group without liver disease and no significant difference is seen between the two groups concerning serum vitamin D levels. So, it can be concluded that serum ammonia level is a better indicator of the presence of liver disease in alcoholic dependence patients than vitamin D.

AUTHOR CONTRIBUTIONS

SG: Conceiving the research question and designing the study plan, compiling of review literature, selection of inclusion and exclusion criteria of study groups; **BBT:** Analysis of the results obtained from the study and correspondence with publisher; **SM:** Collection of samples from study group, processing of samples, and compilation of the data; **SJSC:** Identification of study group, collection and processing of samples from the study group; **DL:** Statistical analysis of the data obtained.

REFERENCES

1. National Institute on Alcohol Abuse and Alcoholism. Alcohol use disorder: a comparison between DSM–IV and DSM–5 [Internet]. 2021 Apr [cited 2023 Nov 2]. Available from: https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/alcohol-use-disorder-comparison-between-dsm

2. American Psychiatric Association. The diagnostic and statical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
3. Zakhari S. Overview: how is alcohol metabolized by the body? Alcohol Res Health. 2006;29:245-54.
4. McCullough AJ, O'Connor JF. Alcoholic liver disease: proposed recommendations for the American College of Gastroenterology. Am J Gastroenterol. 1998;93:2022-36.
5. Schenker S, Breen KJ, Hoyumpa AM Jr. Hepatic encephalopathy: current status. Gastroenterology. 1974;66:121-51.
6. Walker CO, Schenker S. Pathogenesis of hepatic encephalopathy--with special reference to the role of ammonia. Am J Clin Nutr. 1970;23:619-32.
7. Menkes JH, Batzdorf U, Kinsbourne M. Textbook of child neurology. Philadelphia: Lea & Febiger; 1974.
8. Brown T, Hug G, Lansky L, Bove K, Scheve A, Ryan M, *et al*. Transiently reduced activity of carbamyl phosphate synthetase and ornithine transcarbamylase in liver of children with Reye's syndrome. N Engl J Med. 1976;294:861-7.
9. McDermott WV Jr. Metabolism and toxicity of ammonia. N Engl J Med. 1957;257:1076-81.
10. Lowenstein JM. Ammonia production in muscle and other tissues: the purine nucleotide cycle. Physiol Rev. 1972;52:382-414.
11. Duda GD, Handler P. Kinetics of ammonia metabolism in vivo. J Biol Chem. 1958;232:303-14.
12. Stein TP, Leskiw MJ, Wallace HW. Metabolism of parenterally administered ammonia. J Surg Res. 1976;21:17-20.
13. Lockwood AH, McDonald JM, Reiman RE, Gelbard AS, Laughlin JS, Duffy TE, *et al*. The dynamics of ammonia metabolism in man. Effects of liver disease and hyperammonemia. J Clin Invest. 1979;63:449-60.
14. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc. 2006;81:353-73.
15. Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. Am J Clin Nutr. 1998;68(2 Suppl):447S-463S.
16. Upadhyay R, Bleck TP, Busl KM. Hyperammonemia: what urea-lly need to know: case report of severe noncirrhotic hyperammonemic encephalopathy and review of the literature. Case Rep Med. 2016;2016:8512721.
17. Olde Damink SW, Jalan R, Dejong CH. Interorgan ammonia trafficking in liver disease. Metab Brain Dis. 2009;24:169-81.
18. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Washington (DC): National Academies Press (US); 2011.
19. Patel R, Mueller M. Alcohol-associated liver disease. In: StatPearls [Internet]. 2023 Jul 13 [cited 2023 Nov 2]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546632
20. Nair S. Vitamin d deficiency and liver disease. Gastroenterol Hepatol (N Y). 2010;6:491-3.
21. Ravaioli F, Pivetti A, Di Marco L, Chrysanthi C, Frassanito G, Pambianco M, *et al*. Role of vitamin D in liver disease and complications of advanced chronic liver disease. Int J Mol Sci. 2022;23:9016.

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