



TG: HDL, AST: ALT, A:G Ratios in Alcoholic and Non-alcoholic Fatty Liver patients

Abhinav Manish¹, Anuradha Bharosay^{2*}, Kanchan Negi³, Ritesh Srivastava⁴

¹ Assistant Professor, Department of Biochemistry, GBCM Jhajra Dehradun Uttarakhand 248007, India

² Professor & H.O.D, Department of Biochemistry, GBCM Jhajra Dehradun Uttarakhand 248007, India

³ Department of Biochemistry, GBCM Jhajra Dehradun Uttarakhand 248007, India

⁴ Assistant Professor, Department of Biochemistry, GBCM Jhajra Dehradun Uttarakhand 248007, India

*Corresponding author: Dr Anuradha Bharosay, Address: Department of Biochemistry, GBCM Jhajra, Dehradun Uttarakhand 248007, Email:bharosayanuradha@gmail.com, Tel: +919179314919

Abstract

Background & Aims: Nonalcoholic fatty liver disease (NAFLD) is typically first suspected when the results of liver function tests, measured as part of routine testing, are abnormal. Most often observed biochemical pattern in hepatic steatosis due to NAFLD is of increased levels of transaminases, with alanine aminotransferase (ALT) levels exceeding those of aspartate aminotransferase (AST). This classical pattern is particularly useful in differentiating between hepatic steatosis from NAFLD. The pathophysiology of non-metabolic complication like atherosclerosis and cardiovascular disease (CVD) depends vastly on fatty acids (lipid) transportation and Deposition. AIM Estimation of the AST: ALT, Albumin: Globulin, and TG: HDL ratios, along with their comparison among the Alcoholic and Non-alcoholic fatty liver disease patient.

Materials & Methods: A prospective observational cohort study was conducted in the department of Biochemistry at GBCM & KKBM Subharti hospital, Jhajra, Dehradun after obtaining the ethical clearance from the institutional ethical committee (IEC) with registration no GBCM/IEC/2023/07-03 dated 25/07/2023. Cases comprised of 120 Ultrasonographically confirmed fatty liver patients by Random sampling method. 5ml blood sample was collected in the serum separation test tube (SST) and results were analysed using SPSS v.20. and statistical p-value of <0.05 was considered to be significant.

Results: Extremely significant difference in TG: HDL and A:G ratio was found between two groups with statistical p-value of <0.05 and <0.01 respectively.

Conclusion: This study can significantly contribute in evaluating the lipid derangements in two groups and their management.

Keywords: Alcoholic fatty liver, AST: ALT ratio, A: G ratio, Fatty Liver, TG: HDL ratio, Non-Alcoholic Fatty Liver

Received 20 April 2024; accepted for publication 25 July 2024

Introduction

Excess fat deposition within the liver has been recognized for centuries. In a landmark paper published by Ludwig et al, the term “non-alcoholic steatohepatitis (NASH)” was first used to describe the liver histology

associated with excess liver fat in the absence of significant alcohol consumption.(1) Prevalence of NAFLD has doubled over the past 20 years, while prevalence of other chronic diseases of the liver has remained constant and even diminished.(2) Prevalence

of NAFLD in the world is about 25%, (3) in non-obese Asian-Pacific individuals, it is 15–21%, (4) in American adults, it is 30%, and in Italy, it has been reported to be 25%. (5) The term “non-alcoholic” used by the researchers was derived from similarities in the histopathological findings of these patients compared to those with alcohol-related liver disease, due to the lack of knowledge about its pathophysiological basis at that time. Since the introduction of the term nonalcoholic fatty liver disease (NAFLD) into the medical compendium. The pathogenesis of nonalcoholic fatty liver disease remains poorly understood. It is a complex, multifactorial process that involves genetic and environmental elements. (6,7) In early 2020, By an international panel, utilizing a 2-stage Delphi consensus, the term proposed was “metabolic dysfunction-associated fatty liver disease,” or /MAFLD. (8) The pathophysiology of non-metabolic complication like atherosclerosis and cardiovascular disease (CVD) depends vastly on fatty acids (lipid) transportation and Deposition, along with inflammation. Inflammation plays a crucial role in the pathogenesis of cardiovascular disease (CVD), as it has been linked with both the initiation and progression of atherosclerosis (9,10). NAFLD is typically first suspected when the results of liver function tests, measured as part of routine testing, are abnormal. Most often observed biochemical pattern in hepatic steatosis due to NAFLD is of increased levels of transaminases, with alanine aminotransferase (ALT) levels exceeding those of aspartate aminotransferase (AST). This classical pattern is particularly useful in differentiating between hepatic steatosis from NAFLD and alcoholic liver injury, with the latter normally associated with a high AST:ALT ratio. With the progression of hepatic steatosis to NASH and associated hepatic fibrosis, however, AST levels increase with a resultant rise in the AST:ALT ratio. (11) Albumin synthesis is also a function of Liver and Globulin is synthesized outside of liver, A:G ratio and fatty liver relation is very less studied. In cases of fatty liver the role of A:G ratio could be important, so we conduct this study to compare the

TG: HDL, AST: ALT, and A:G Ratios in Alcoholic and Non-alcoholic Fatty Liver patients.

Material & Methodology

Study design: A prospective observational cohort study was conducted in the department of Biochemistry at GBCM & KKBM Subharti hospital, Jhajra, Dehradun after obtaining the ethical clearance from the institutional ethical committee (IEC) with registration no GBCM/IEC/2023/07-03 dated 25/07/2023. Tutor from the Biochemistry department is posted in the Medicine and Surgery OPD for collection of history of the patient from a specified format, and consent of the patient to enrol in the study. A fasting serum sample was preferred.

Sample size and sampling: After taking informed or written consent, 120 Ultrasonographically confirmed fatty liver patients were enrolled in the study. 5ml blood sample was collected in the serum separation test tube (SST) from the patients who visited the medicine as well as surgery outpatient department (OPD) of KKBM Subharti hospital during the period of June–December 2023.

Study procedure: The study group is divided into Alcoholic and Non-alcoholic fatty liver patients. AST:ALT ratio, A:G ratio, and TG:HDL ratio was calculated after obtaining the Liver and Lipid Profile results by using EM-200 fully automated clinical chemistry analyser for both alcoholic fatty liver and Non-alcoholic Fatty Liver Patients. The results were evaluated by using SPSS v.20. The results were expressed as Mean±SD. Statistical means was compared using ‘t’ test and p-value of <0.05 was considered to be significant.

Inclusion criteria:

Ultrasonographically confirmed fatty liver patients among the age group of 20-80 yrs were enrolled in the study.

Exclusion criteria:

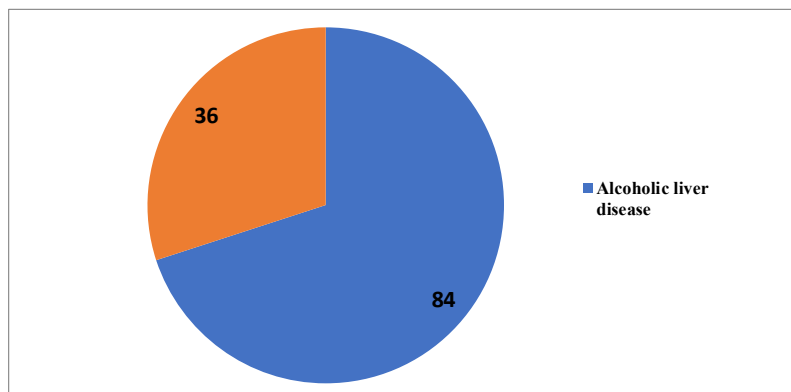
Patients with Diabetes mellitus, hypertension, age less than 20yrs and more than 80yrs, and confirmed endocrinopathies patients were excluded from the study.

Result

Out of 120 fatty liver patients 70% (n=84) were alcoholic liver disease, and 30% (n=36) were Non-alcoholic fatty liver disease. There was a significant difference found between the TG: HDL ratio, AST:ALT ratio, A:G ratios among the ALD and NALD patients with extremely significance p- value of <0.05. The result are as follows:

The mean±sd value for TG:HDL ratio in ALD and NALD was 5.07±3.58 and 3.39±1.96 respectively. The mean±sd value for AST: ALT ratio in ALD and NALD was 0.99±0.70 and 1.18±0.53 respectively. The mean±sd value for A: G ratio in ALD and NALD was 1.49±0.45 and 1.79±0.38 respectively.

These results are tabulated below in Table 1 and represented graphically in Graph 1 and Graph 2.

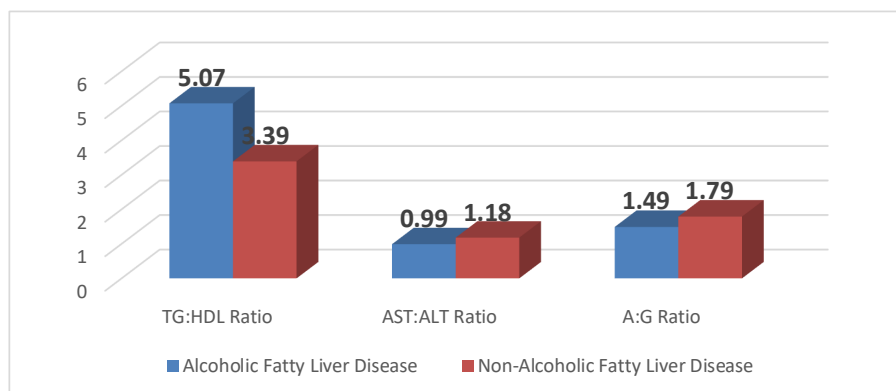


Graph 1. Frequency of fatty liver patients on the basis of alcohol consumption

Table 1. Comparison among the Alcoholic and Non-alcoholic Fatty Liver Disease

S.no	Parameters	Alcoholic liver disease (mean±sd) N=84	Non-alcoholic liver disease (mean±sd) N=36	*P-value	Significance
1.	TG: HDL Ratio	5.07±3.58	3.39±1.96	0.009	ES
2.	AST: ALT Ratio	0.99±0.70	1.18±0.53	0.01	ES
3.	A: G Ratio	1.49±0.45	1.79±0.38	<0.001	ES

*P<0.05 represents statistically significant values, AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; A:G Albumin: Globulin.



Graph 2. Comparison among the Alcoholic and Non-alcoholic Fatty Liver Disease

Discussion

There is limited historical evidence for the recognition of NAFLD and its contributory factors in the literature. Evidence that is available suggests that NAFLD recognition and diagnosis in primary care settings that manage the majority of patients are poorly understood and applied. The simple criteria for FLD (AFLD and NAFLD) have been purported to increase the recognition and understanding outside of gastroenterology and hepatology specialists, and it will also enable primary care practitioners and others to initiate early management. (12) The ratio of the serum activities of AST and ALT, also known as the De Ritis ratio, was first described by Fernando De Ritis in 1957. (13) It is commonly used to assess liver function and reflects the severity of liver disease. Previous studies reported that AST/ALT was more helpful for identifying heavy drinking in the NHANES study than when they were used alone (14). Our results provide a strong comparison result, which can aid in the diagnosis of fatty liver cause whether it is alcoholic or non-alcoholic, so it can help in the initial treatment planning. Satter Naved et al. (15) in his study represents most patients with NAFLD are asymptomatic and the disease is typically suspected based on raised alanine aminotransferase (ALT) levels together with other clinical and biochemical features, or an incidental finding during abdominal ultrasonography, these results are in accordance with our study. In a study by Arora et al. (16) showed highly significant increase in the levels of AST/ALT ratio in alcoholic liver disease patients as compared to control group. These results are found to be opposite of our results which could possibly be due to the fact that the comparison they have conducted is with healthy controls but our study includes the cohort of fatty liver patients and these patients although are non-alcoholic but having fatty liver which is Ultrasonographically confirmed. Nyblom et al. (17) also demonstrated the similar results with alcoholic liver disease with AST/ALT ratio of 1.0 ± 0.6 (patients with withdrawal symptoms due to alcoholism) $1.7 \pm 1.0^*$ (patients with somatic diagnoses in addition to a diagnosis of alcohol abuse or dependence) our results

are for alcoholic fatty liver disease (0.99 ± 0.70) and for Non-alcoholic liver disease is (1.18 ± 0.53) these results are in accordance with our study. Bayard M. et al. (18) demonstrated in his study that laboratory abnormalities often are the only sign of NAFLD. Most commonly elevated liver enzymes are alanine transaminases (ALT) and aspartate transaminases (AST), usually one to four times the upper limits of normal. The ratio of AST/ALT usually is less than 1 (in alcoholic liver disease) but may increase as the severity of the liver damage increases. These findings are in accordance with our results and validate our study results.

Conclusion

There is an extremely significant difference found between the Alcoholic and Non-alcoholic Fatty Liver disease in the TG: HDL, A: G ratios were found to be most significant. In the literature the Albumin alone or combined with liver function tests panel is found to be significant in fatty liver but it would not be sufficient to comment on the status of alcohol involvement but A:G ratio in fatty liver could be a promising marker for differentiation among alcoholic and non-alcoholic fatty liver. Study group is confined to the Uttarakhand region only, so geographical variation could be the limitation, which requires more external validity, also similar multicentric studies with large cohort groups would bring more light to it.

Acknowledgement

The authors are grateful to Hon. Chairman, Gautam Buddha Chikitsa Mahavidyalaya (GBCM) for his constant support in pursuing such research work in central diagnostic laboratory. We are also thankful to the staff of the Department of Biochemistry, GBCM for their technical assistance.

Ethical approval

The study was conducted in accordance with the ethical standards set forth by the institutional ethical committee (IEC) of GBCM & KKBM Subharti hospital, Jhajra, Dehradun. Ethical clearance was obtained with

registration number GBCM/IEC/2023/07-03, dated 25/07/2023.

This research work is registered under CTRI (Clinical Trial Registry – India) /ICMR (Indian Council of Medical Research) with registration number CTRI/2023/11/059450.

Data Availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

Conflicts of interest

There are no conflicts of interest.

Financial support/grant received

The financial support is provided by Gautam Buddha Chikitsa Mahavidyalaya, Jhajra Dehradun, Uttarakhand 248007 for the sample analysis.

References

- Ludwig J, Viggiano TR, McGill DB, Oh B. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc* 1980;55(7):434-8.
- LaBrecque DR, Abbas Z, Anania F, Ferenci P, Khan AG, Goh K-L, et al. World Gastroenterology Organisation global guidelines: Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. *J Clin Gastroenterol* 2014;48:467-73. <https://doi.org/10.1097/MCG.0000000000000116>
- Araújo AR, Rosso N, Bedogni G, Tiribelli C, Bellentani S. Global epidemiology of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis: What we need in the future. *Liver Int* 2018;38:47-51. <https://doi.org/10.1111/liv.13643>
- Chun Jen L. Prevalence and risk factors for non-alcoholic fatty liver disease in Asian people who are not obese. *J Gastroenterol Hepatol* 2012;27:1555-60. <https://doi.org/10.1111/j.1440-1746.2012.07222.x>
- Bellentani S, Scaglioni F, Marino M, Bedogni G. Epidemiology of non-alcoholic fatty liver disease. *Dig Dis* 2010;28:155-61. <https://doi.org/10.1159/000282080>
- Angulo P, Lindor KD. Non-alcoholic fatty liver disease. *J Gastroenterol Hepatol* 2002;17 Suppl:S186-90. <https://doi.org/10.1046/j.1440-1746.17.s1.10.x>
- Harrison SA, Kadam S, Lang KA, Schenker S. Nonalcoholic steatohepatitis: what we know in the new millennium. *Am J Gastroenterol* 2002;97(11):2714-24. <https://doi.org/10.1111/j.1572-0241.2002.07069.x>
- Goffon C, Upendran Y, Zheng MH, George J. MAFLD: How is it different from NAFLD? *Clin Mol Hepatol* 2023 Feb;29(Suppl):S17-S31. <https://doi.org/10.3350/cmh.2022.0367>
- Christodoulidis G, Vittorio TJ, Fudim M, Lerakis S, Kosmas CE. Inflammation in coronary artery disease. *Cardiol Rev* 2014;22:279-288. <https://doi.org/10.1097/CRD.0000000000000006>
- Kosmas CE, Silverio D, Sourlas A, Montan PD, Guzman E, Garcia MJ. Anti-inflammatory therapy for cardiovascular disease. *Ann Transl Med.* 2019;7:147. <https://doi.org/10.21037/atm.2019.02.34>
- Sorbi D, Boynton J, Lindor KD. The ratio of aspartate aminotransferase to alanine aminotransferase: Potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. *Am J Gastroenterol* 1999;94:1018-22. <https://doi.org/10.1111/j.1572-0241.1999.01006.x>
- Shiha G, Korenjak M, Eskridge W, Casanovas T, Velez-Moller P, Höglström S, et al. Redefining fatty liver disease: An international patient perspective. *Lancet Gastroenterol Hepatol* 2021;6:73-79. [https://doi.org/10.1016/S2468-1253\(20\)30294-6](https://doi.org/10.1016/S2468-1253(20)30294-6)
- De Ritis F, Coltrati M, Giusti G. An enzymic test for the diagnosis of viral hepatitis: the transaminase serum activities. *Clin Chim Acta* 1957;2:70-4. [https://doi.org/10.1016/0009-8981\(57\)90027-X](https://doi.org/10.1016/0009-8981(57)90027-X)
- Kim SG, Kim HY, Seo JA, Lee KW, Oh JH, Kim NH, et al. Relationship between serum adiponectin concentration, pulse wave velocity, and nonalcoholic fatty liver disease. *Eur J Endocrinol* 2005;152:225-31. <https://doi.org/10.1530/eje.1.01842>
- Sattar N, Forrest E, Preiss D. Non-alcoholic fatty liver disease. *BMJ* 2014 Jul 29;349:g4596. <https://doi.org/10.1136/bmj.g4596>

-
16. Arora M, Mahat R, Kumar S, Sharma A, Batra J. Evaluation of AST/ALT Ratio in patients of alcoholic Liver Disease. *Bull Pharm Med Sci* 2015;vol 3:3027-30.
 17. Nyblom H, Berggren U, Balldin J, Olsson R. High AST/ALT ratio may indicate advanced alcoholic liver disease rather than heavy drinking. *Alcohol Alcohol* 2004;39(4):336-39.
<https://doi.org/10.1093/alcalc/agh074>
 18. Bayard M, Holt J, Boroughs E. Nonalcoholic fatty liver disease. *Am Fam Physician* 2006 Jun 1;73(11):1961-8.

This is an open-access article distributed under the terms of the [Creative Commons Attribution-noncommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, as long as the original work is properly cited.