Original Article JCMCTA 2024 ; 35 (2) : 95-99

Non-Alcoholic Fatty Liver Disease: Relation of Hepatic Enzymes with Obesity and Lipid Profile

Sheley Akter[1*]

Abstract

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is the leading chronic liver disease worldwide. Early diagnosis is crucial to manage NAFLD timely. This study was aimed to evaluate the changes in hepatic enzymes in patients with NAFLD and determine the relation of hepatic enzymes with obesity and lipid profile.

Materials and methods: This descriptive cross-sectional study was conducted in the Department of Physiology in Chittagong Medical College Hospital from June 2016 to September 2016. Seventy-five subjects with NAFLD on ultrasonography were included from the Department of Radiology of Chittagong Medical College Hospital. Participants were subjected to anthropometric and clinical examinations. Liver enzymes- Serum Alanine aminotransferase (ALT) Aspartate Aminotransferase (AST) were estimated according to the standard guideline.

Results: Liver enzyme ALT and AST were elevated respectively in 68% and 44% of the NAFLD patients. Mean values were also higher than the normal referral range. Both ALT and AST were significantly higher in older patients with higher BMI (≥25 kg/m^2) in patients with high cholesterol, Triglyceride (TG) and Low- Density Lipoprotein (LDL) ($p<0.05$). Both ALT and AST level showed a significant positive correlation with serum cholesterol, TG and LDL but only serum ALT showed a strong positive correlation with BMI.

Conclusion: The study suggested that liver enzyme levels alter in NAFLD patients and also highlighted the importance of age, BMI, and dyslipidemia to assess individuals risk for NAFLD, which reaffirms the connection to the disease.

Key words: Fatty liver; Hepatic enzyme; Lipid profile; Obesity.

Introduction

NAFLD is one of the most common cause of chronic liver disease globally.[1] It covers a wide range of disorders ranging from simple fat accumulation or steatosis in the liver and hepatic inflammation (Steatohepatitis) to development of fibrosis and even cirrhosis.[2,3] According to a study report, almost one-third of the population in Bangladesh suffered from NAFLD.[4] This finding outlines the nation's severe NAFLD pandemic and emphasizes the added risk of rising liver-related mortality and morbidity.[4]

Obesity, diabetes mellitus, and dyslipidemia are frequent metabolic comorbidities associated with Non-Alcoholic Fatty Liver Disease (NAFLD) in most patients.[5]

NAFLD patients may have elevated serum Alanine Aminotransferase (ALT) serum Aspartate Aminotransferase (AST) and Gamma Glutamyl Transferase (GGT).[6] Serum ALT, AST, GGT are markers of liver injury and ALT is more specific for liver disease.[7] ALT is closely associated with accumulation of fat in the liver and higher ALT concentration is associated with the degree of steatosis.[8] Elevated ALT levels was found to be associated with NAFLD clinically and histologically.[9] ALT is frequently used as surrogate marker for NAFLD in epidemiological research.[7] But according to World Gastroenterology Organization (WGO) ALT and AST were found normal in about 10% of NASH patients having simple steatosis.[10]

In various studies significant association of numerous factors were found with NAFLD.[2,6,11,12] By controlling these factors further progression of the disease process can be stopped with reduction of mortality and morbidity. There are limited studies on hepatic enzymes concerning other predictive variables of NAFLD in our country. So, the present study was designed to see the changes in liver enzymes, especially ALT and AST, in patients of USG positive NAFLD and their relation with other variables related to NAFLD to identify patients at risk of disease progression.

Materials and methods

This descriptive cross-sectional study was conducted in the Department of Physiology in Chittagong Medical College from June 2016 to

1. Assistant Professor of Physiology
Chittagong Medical College, Chattogram.

***Correspondence:** **Dr Sheley Akter**
Cell : 01819 33 45 32
E-mail: drsheleyakter34@gmail.com

Submitted on : 10.06.2024
Accepted on : 12.07.2024

September 2016. Prior to data collection, written consent was taken from each individual. Ethical approval was obtained from the Ethical Review Committee of Chittagong Medical College.

Seventy-five subjects, sonologically diagnosed as NAFLD, aged from 18 years to 65 years were included. Patients with a history of alcohol consumption, acute or chronic liver disease, and receiving steatogenic drugs were excluded. Patient's age, sex were recorded, height, weight and blood pressure were measured by standard methods, and recorded in a pretested structured data collection sheet. About 5 ml of fasting blood specimen was collected from every individual, processed, and analyzed for blood chemistry parameters. Serum ALT and AST level, fasting lipid profile (Cholesterol, triglyceride, LDL-C, HDL-C) were measured by using standard techniques.

Diagnosis of NAFLD was done by Ultrasonography which was performed by an experienced Radiologist in the Radiology and Imaging Department of Chittagong Medical College Hospital by MedisonSonoAce R7 ultrasound machine. Ultrasonography has a sensitivity of 60% to 94% and a specificity of 84% to 95% for detecting fatty liver[13]. Obesity and overweight were classified based on Body Mass Index (BMI): Normal: 18.5-24.9 kg/m^2, over weight: 25-29.9kg/m^2 and obese: ≥30.0 kg/m^2.[14] The normal range for ALT and AST was respectively 10-40 IU/L and 10-35 IU/L as provided by reagent manufacturer's guideline.[7]

Data analysis was done with SPSS version 20. Quantitative data were expressed in mean ± SD and were analyzed by Student's t-test. Qualitative data were analyzed by Chi-square test. Pearson's correlation coefficient was calculated to determine the correlation between liver enzymes with other variables. p< 0.05 was considered statistically significant.

Results

Among 75 study participants, 52% were male, and 48% were female. The meanage of the study population was 43.13±9.5 years. Mean BMI was 27.8±12.3 and 82.6% of NAFLD patients had BMI ≥25 kg/m^2. Both mean ALT and AST level were above normal referral range. Serum ALT was elevated in 68% and serum AST was elevated in 44% of patients (Table I).

Table I Demographic, clinical and biochemical findings of the patients (n=75)

Characteristics	Mean±SD
Age (Years)	43.1±9.5
BMI (kg/m^2)	27.8±12.3
Total cholesterol (mg/dl)	167.3 ± 29.0
Triglyceride (mg/dl)	194.2 ± 35.4
Low density lipoprotein (mg/dl)	111.0 ± 19.7
High density lipoprotein (mg/dl)	38.4 ± 9.0
ALT(IU/L)	51.6 ± 19.2
AST(IU/L)	36.7 ± 13.6
AST / ALT	0.73 ± 0.14

Table II shows that both serum elevated ALT level and elevated AST level were significantly associated with age, BMI, TC,TG and LDL-Clevel.

Table II Association of ALT and AST status with different variables

	ALT level			AST level		
Variables	Elevated (n=51)	Normal (n=24)	p value	Elevated (n=33)	Normal (n=38)	p value
Age, years	45.6±10.3	41.9±8.9	0.048	44.4±9.7	41.4±9.1	0.045
Malesex	30 (58.9)	9 (37.5)	0.056	20 (60.6)	19 (50.0)	0.186
BMI, ≥25kg/m^2	43 (84.3)	19 (79.2)	0.043	32 (96.7)	30 (78.9)	0.049
TC, mg/dl	174.9±27.9	152.1±25.6	0.001	178.7±28.7	150.3±27.9	0.001
TG, mg/dl	204.1±32.1	174.6±33.9	0.001	200.6±30.8	184.5±36.1	0.001
LDL-C,mg/dl	113.5±20.8	106.1±16.7	0.025	114.9±17.8	97.9±20.8	0.025
HDL-C,mg/dl	38.8±10.8	37.4±6.55	0.519	39.8±11.7	37.2±6.0	0.619

p values were derived from either Chi-square test or independent sample 't' test.

Table III shows a significant positive correlation of serum ALT with BMI, TC, TG and LDL-C. A significant positive correlation of serum AST with TC, TG and LDL- C was observed in the NAFLD patients.

Table III Correlation of ALT and AST with other variables

	ALT (IU/L)		AST (IU/L)	
Variables	rvalue	p value	rvalue	p value
BMI (kg/m^2)	0.275	0.017	0.162	0.166
Cholesterol (mg/dl)	0.394	<0.001	0.366	0.001
Triglyceride (mg/dl)	0.477	<0.001	0.368	0.001
LDL-C (mg/dl)	0.269	0.020	0.273	0.018
HDL-C (mg/dl)	0.036	0.759	0.053	0.648

r: Pearson's correlation coefficient.

Discussion

NAFLD is a global health problem and the prevalence among adults is estimated tobe 23–25%.[1,4] The present study was conducted to evaluate the changes of hepatic enzymes, especially ALT and AST, in patients with

sonologically positive NAFLD. Attempts were made to observe the correlation of ALT and AST level with BMI and serum lipid profile.

In the present study, patients with elevated liver enzymes had significantly higher age. which was consistent with the previous studies.[4,7,10,11,12,15,16]

Aging is associated with various liver diseases including NAFLD.[17]

In the present study, serum ALT and AST levels were above the normal referral range, respectively, in 68% and 44% of the NAFLD cases. Mean values were also higher than the normal referral range. A one-to three-fold rise in liver enzyme serum ALT, is frequently the first sign of non-alcoholic fatty liver disease (NAFLD).[18] As ALT increases more than AST, the AST to ALT ratio is usually less than one, which was consistent with previous studies.[11,18,]

One important risk factor for NAFLD is obesity.[19,20] In ourstudy, about 82% of NAFLD patients were over weight or obese (≥25 kg/m2). Marked elevation of both ALT and AST was found in patients with higher BMI. Significant association between elevated liver enzyme ALT, AST and BMI was found in several studies.[11.21] In obese individuals increased risk of ALT was found several times higher.[22,23]

Dyslipidemia was known to be an essential risk factor for NAFLD.[19,24] In our study, serum ALT and AST levels were significantly elevated in NAFLD patients with higher serum cholesterol, TG and LDL. In several studies, very high predominance of elevated liver enzymes were found among participants who were dyslipidemic.[25,26] Zakeri and Karmarat-Panah stated that ALT and dyslipidemia might be involved in the prevalence and development of NAFLD.[27] According to Williamson et al. BMI and triglycerides were independent indictors of NAFLD.[24] Hyper triglyceridemia was more significantly associated with hyper cholesterolemia in several studies but few studies established that hypercholesterolemia causes NAFLD.[28-30] According to some research, low HDL-C and hyper triglyceridemia were found to be risk factors for NAFLD development.[31, 32]

On correlation analysis, both ALT and AST levels showed a significant positive correlation with serum cholesterol, TG, LDL but correlation with HDL was not significant. In the study of Al-Jameil et al., cholesterol, TG, LDL had a strong positive correlation with ALT but AST showed weak relation with all parameters.[33] A significant positive correlation was observed between serum ALT and BMI, but AST level showed a non significant positive correlation with BMI which is consistant with several studies.[11,23]

This study focused light on the correlation between hepatic enzymes and other risk factors in NAFLD patients within a particular geographic area, which may be valuable information for managing and monitoring NAFLD.

Limitations

The current study used a small sample size and was a time-framed cross-sectional study conducted in a small context. NAFLD was diagnosed only on the basis of hepatic steatosis imaging; a liver biopsy was not performed to confirm the presence of fibrosis or cirrhosis.

Conclusion

In conclusion, this study reveals an elevation of hepatic enzyme, ALT and AST in NAFLD patients. Obesity and dyslipidemia play a significant role in changes in ALT and AST. So, these enzymes should be evaluated in NAFLD patients.

Recommendation

Extensive research is required to clarify the causal connection between hepatic enzymes and other characteristics of nonalcoholic fatty liver disease. Furthermore, researching the frequency of NAFLD in the general population is crucial to monitor the disease epidemiology.

Acknowledgement

The author expressed her gratitude to the staff of Department of Physiology & Radiology, CMCH.

Contribution of author

The whole worked conducted by the author herself.

Disclosure

The author declared no conflict of interest.

References

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L,Wymer M. Global epidemiologyof non alcoholic fatty liver disease—meta analytic assessment of prevalence, incidence and outcomes. Hepatology. 2016;64(1):73-84.

2. Chalasani N, Younossi Z, Lavine J, Diehl A, Cusi K, Charlton M et al. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guideline by the American Association for the study of Liver Diseases. American College of Gastroenterology and the American Gastroenterological Association 2012;55(6):2005-2023.

3. Goh GB, Pagadala MR, Dasarathy J, Unalp-Arida A, Sargent R, Hawkins C et al. Clinical spectrum of non-alcoholic fatty liver disease in diabetic andnon-diabetic patients. BBA clinical. 2015;3:141-145.

4. Alam S, Fahim SM, Chowdhury MA, Hassan MZ, Azam G, Mustafa G, et al. Prevalence and risk factors of non‑alcoholicfatty liver disease in Bangladesh. JGH Open. 2018;2(2):39-46.

5. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison SA, Brunt EM, Sanyal AJ. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67:328–357

6. Khammas AS, Hassan HA, Salih SQ, Kadir H, Ibrahim RM, Nasir NN, et al. Prevalence and risk factors of sonographically detected nonalcoholic fattyliver disease in a screening center in Klang Valley, Malaysia: an observational cross-sectional study. Porto biomedical journal. 2019;4(2):12-16.

7. Debmalya Sanyal, Pradip M, Moutusi R, Sujoy G, Satinath M, Subhankar C. Profile of liver enzymes in non-alcoholic fatty liver disease in patients with impaired glucose tolerance and newly detected untreated type 2 diabetes.Indian Journal of Endocrinology and Metabolism. 2015 Sep-Oct;19(5): 597-601.

8. Rocha R, Cotrim HP, Bitencourt AGV, Barbosa DBV, Santos AS, Almeida ADM, et al.Nonalcoholic fatty liver disease in asymptomatic Brazilian adolescents, World J Gastroenterology. 2009;15:473-477.

9. Bi WR, Yang CQ, Shi Q, Xu Y, Cao CP, Ling J, Wang XY. Large-scale analysis of factors influencing nonalcoholic fatty liver disease and its relationship with liver enzymes. Genet Mol Res. 2014;13(3):5880–5891.

10. Douglas L, Zaigham A, Frank A, Peter F, Aamir G, Khean-Lee G et al. Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. World Gastroenterology Organization Global Guidelines. 2012; 1:1-29.

11. Noor F, Shorovi N, Sarwar S, et al. Prevalence and Associated Factors of Liver Enzyme Abnormalities Among Bangladeshi Women: A Cross-Sectional Study. Cureus. 2024;16(4): e57606.

12. Ali N, Sumon AH, Fariha KA et al. Assessment of the relationship of serum liver enzymes activity with general and abdominal obesity in an urban Bangladeshi population. Sci Rep. 2021;11:6640.

13. Marjia G P, Marko D, Neven B, Ultrasonography in the diagnosis of nonalcoholic fatty liver disease. 2009;63(3):1-3.

14. Body mass index: Introduction and History to BMI. Body Mass Index /BMI Calculator 2015. http:/bmicalculator.cc/body-mass-index.

15. Shivaram PS, Ayashkanta S, Debasis M, Bijoy M, Girish KP, Manas KP et el. Risk factors associated with non-alcoholic fatty liver disease in Indians, A case control study. J Clin Exp Hepatol. 2015;5(4):295-302.

16. Shahinul A, Sheikh M-E-A, Ziaur RC, Mahabubul AJK, Nonalcoholic steato hepatitis in nonalcoholic fatty liver disease patients of Bangladesh. World Journal of Hepatol. 2013;5(5):281-287.

17. Kim IH, Kisseleva T, Brenner DA. Aging and liver disease. Curr Opin Gastroenterol. 2015;31(3):184-191.

18. Lonardo A, Nascimbeni F, Ballestri S, Fairweather D, Win S, Than TA, et al. Sex Differences in Nonalcoholic Fatty Liver Disease: State of the Art and Identification of Research Gaps. Hepatology. 2019;70(4):1457-1469.

19. Bimol CS, Madhusudan S, Faruque A, Swapan CD. Non-Alcoholic Fatty Liver disease: Study of Demographic and Predictive factors. Euroasian Journal of Hepato-Gastroenterology. 2015;5(1):4-6.

20. Shiraz S, Khan, Nishad S.K, Sagor S. P, Vijoy M. K. Association of non-alcoholic fatty liver disease with anthropometric and metabolic parameters in type 2 diabetes: A retrospective analysis. Int J Res Med Sci. 2017;5(1):225-230.

21. Nurshad A, Abu H S, Khandaker AF, Md AZ, Rahanuma RK, Noyan H M, et al. Assessment of the relationship of serum liver enzymes activity with general and abdominal obesity in an urban Bangladeshi population.National Library of Medicine.2021; 11: 6640.

22. Nurshad A, Sumon AH, Fariha KA, Asaduzzaman M, Kathak RR et al. Assessment of the relationship of serum liver enzymes activity with general and abdominal obesity in an urban Bangladeshi population.. National Library of Medicine. 2021;11:6640.

23. Adams LA, Knuiman MW, Divitini ML, Olynyk JK. Body mass index is a stronger predictor of alanine aminotransaminase levels than alcohol consumption. J. Gastroenterol. Hepatol. 2008;23:1089–1093.

24. Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Contreras M, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. Gastroenterology. 2011;140:124-131.

25. Rehnuma RK, Suman A H, Mollah NH, Hassan M, Miah R, Tuba H et al. The association between elevated lipid profile and liver enzymes: A study on Bangladeshi adults. National Library of Medicine. 2022; 12: 1711.

26. De Souza, L. J. et al. Prevalence of dyslipidemia and risk factors in Campos dos Goytacazes, in the Brazilian State of Rio de Janeiro. Arq. Bras. Cardiol.2003;81: 257–264.

27. Zakeri A, Karamat-Panah S. Prevalence of non-alcoholic fatty liver disease and its risk factors in patients referred to Ardabil city hospital during 2015-2016. Int J Community Med Pub Health. 2018; 5:917–921.

28. Cheah WL, Lee PY, Chang CT, Mohamed HJ, Wong SL. Prevalence of ultrasound diagnosed nonalcoholic fatty liver disease among rural indigenous community of Sarawak and its association with biochemical and anthropometric measures. Southeast Asian J Trop Med Public Health. 2013;44(2):309-317.

29. Mahtab AM, Sheikh MFA. Nonalcoholic fatty liver disease: A review. Journal Gastroentrol and Hepatol. 2013;2(3):330-353.

30. Ma KL, Ruan XZ, Powis SH, et al. Inflammatory stress exacerbates lipid accumulation in hepatic cells and fatty livers of apolipoprotein E knockout mice. Hepatology.2008;48:770–771.

31. Goh S, Ho EL, Goh K. Prevalence and risk factors of non-alcoholic fatty liver disease in a multiracial suburban Asian population in Malaysia. Hepatol Int.2013;7:548–554.

32. Lee L, Alloosh M, Saxena R, et al. Nutritional model of steatohepatitis and metabolic syndrome in the Ossabaw miniature swine. Hepatology. 2009;50:56–57.

33. Al-Jameil N, Khan FA, Arjumand S, Khan MF, Tabassum H. Associated liver enzymes with hyperlipidemic profile in type 2 diabetes patients. International journal of clinical and experimental pathology. 2014;7(7):4345-4349.