Original Article

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Profile of Liver Enzymes in Non-Alcoholic Fatty Liver Disease: Relation with Type 2 Diabetes Mellitus and Hypertension

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Abstract

Background: Non Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease worldwide. It is frequently associated with obesity, type 2 Diabetes Mellitus (DM) dyslipidemia and Hypertension (HTN). NAFLD patients may have higher level of serum Alanine Aminotransferase (ALT) serum Aspartate Aminotransferase (AST) or both. The aim of our study was to assess the profile of hepatic enzymes, specially serum ALT and AST in patients with USG-diagnosed NAFLD with regards to presence or absence of DM and HTN.

Materials and methods: This cross sectional observational study was conducted in the Department of Physiology, Chittagong Medical College (CMC) during the period of January 2016 to December 2016. Total seventy five subjects, having fatty liver disease on ultrasonography, done by Radiologist of CMCH and fulfilling the inclusion and exclusion criteria were included in the study. Anthropometric measurments and clinical examinations were done. Serum ALT and serum AST level, Fasting Blood Glucose (FBS) and 2 Hrs Post Prandial Blood Glucose (2HPPBS) were estimated according to standard guideline. Data analysis was done by computer based software SPSS windows version 20. Data were expressed in mean ± SD. Students "t" test and chi-square test were done.

Results: Liver enzyme ALT and AST were found elevated in 68% and 44% of the NAFLD patients respectively. Mean (± SD) ALT and AST were also higher than normal. Both ALT and AST were significantly higher in older patients with type II diabetes mellitus and hypertension. Only ALT elevation was significantly associated with systolic blood pressure.

Conclusion: This study revealed that hepatic enzymes, ALT and AST elevate in NAFLD patients and also highlighted the importance of Type 2 Diabetes mellitus, hypertension to assess everyones risk for NAFLD. So, these enzymes should also be evaluated in NAFLD patients.

Key words: Hypertension; Liver enzyme; Non-alcoholic fatty liver disease; Type 2 diabetes mellitus.

Introduction

NAFLD is the most common liver disorder worldwide.[1] It is a wide range of liver disease from simple hepatic steatosis to steatohepatitis (NASH) and fibrosis with a significant risk of cirrhosis and Hepatocellular Carcinoma (HCC).[1] About 33% of rural adult population of Bangladesh suffer from NAFLD.[2]

NAFLD is considered as the hepatic manifestation of Metabolic Syndrome (MetS).[3] In most studies, the prevalence of NAFLD is higher in individuals with features of metabolic syndrome including obesity, diabetes mellitus, hypertension and an increased waist circumference.[4] NAFLD is now termed as Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD).[5]

The most common presentation of NAFLD is incidental finding of raised ALT and AST, with a preserved ALT: AST ratio of 1.5.[6] Serum ALT and AST can be used to predict the degree of USG diagnosed NAFLD.[7] In epidemiological studies, ALT is frequently used as surrogate marker for NAFLD.[8] In several studies, serum ALT and AST level was significantly higher in NAFLD patients.[9,10,11] But according to World Health Organization (WGO) in about 10% of NASH patients with simple steatosis, ALT and AST level may be normal and similar findings were found in some previous studies.[12,13,14]

Significant association of numerous factors were found with NAFLD in various studies. Presence of T2DM is the most powerful predictive risk factor for hepatic fibrosis even in lean patients with NAFLD.[15] Liver enzymes, especially ALT, were independently associated with NAFLD in a Nepalese population with T2DM.[10] A significant association between high levels of ALT and an

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increased risk of hypertension was found in a study, regardless of other risk factors.[16] Hypertension was significantly associated with NAFLD and was considered as predictor for NASH.[17]

Early detection of hepatic dysfunction through enzyme assessment may help to prevent progression of liver disease. So,this study was aimed to evaluate the profile of liver enzymes, ALT and AST in NAFLD patients and to analyze their association with T2DM and hypertension in the Bangladeshi population to support early screening for disease progression and guide preventive measures accordingly.

Materials and methods

This cross sectional observational study was conducted in the Department of Physiology, Chittagong Medical College (CMC) during the period of January 2016 to December 2016. Ethical approval was obtained from the Ethical Review Committee of Chittagong Medical College.

Study was done on total seventy five patients of 18 years to 65 years with sonologically positive non alcoholic fatty liver disease after fulfilling the inclusion and exclusion criteria. The subjects were selected on the basis of voluntary purposive sampling. Informed written consent was taken from all. Age, sex of all subjects were recorded, height, weight and blood pressure were measured by standard methods and recorded in a pretested structured data collection sheet.

With all aseptic precautions about 5 ml of fasting venous blood was collected from the median cubital vein of all subjects, processed and analysed. Serum ALT and AST level, Fasting Blood Glucose (FBS) were measured by using standard techniques. 2 Hrs Post Prandial Glucose (2HPPBS) level was measured 2 hrs after breakfast.

Diagnosis of NAFLD was done by Ultrasonography, performed in the Radiology and Imaging Department of Chittagong Medical College Hospital by an experienced Radiologist by Medison SonoAce R7 ultrasound machine. A good quality Ultrasound has sensitivity of 90%, a specificity of 46%, a positive predictive value of 77% and and negative predictive value of 66% for diagnosing NAFLD.[18] The normal range for ALT and AST was 10-40 IU/L and 10-35 IU/L respectively, provided by reagent manufacturer guideline.[8] .

Data were analyzed using 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

The mean age of the study population was 43.13±9.5 years. Mean (± SD) ALT and AST were higher than normal referral range.

Table I Demographic, clinical, and biochemical findings (According to mean) (n=75)

Characteristics	Mean±SD
Age (Years)	43.1±9.5
Systolic blood pressure (mm of Hg)	125.67±9.63
Diastolic blood pressure (mm of Hg)	80.3±5.9
Fasting blood glucose (mg/dl)	132.4±38.0
2 hours post prandial blood glucose (mg/dl)	165.3 ± 54.4
ALT (IU/L)	51.6 ± 19.2
AST (IU/L)	36.7 ± 13.6
AST / ALT	0.73 ± 0.14

In our study, 32% of NAFLD patients were reported hypertensive, 43% were reported diabetic. Serum ALT was elevated in 68% and serum AST was elevated in 44% of patients (Table II).

Table II Demographic, clinical, and biochemical findings (According to frequency)(n=75)

Characteristics	Frequency (%)
Gender	
Male	39 (52.0)
Female	36 (48.0)
Reported hypertension	24 (32.0)
Reported diabetes mellitus	32 (43.0)
Elevated ALT	51 (68.0)
Elevated AST	33 (44.0)

Table III shows that both serum ALT and AST elevations were significantly associated with older age, reported diabetes, and reported hypertension in this study. Only serum ALT elevation was significantly associated with systolic blood pressure. Both ALT and AST were not significantly associated with fasting or postprandial blood sugar level.

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Table III Association of ALT and AST status with different variables

Variables	ALT level			AST level		
	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
Reported DM	23 (45.1)	9 (37.5)	0.022	24 (72.7)	8 (21.1)	0.021
Reported HTN	18 (35.3)	6 (25.0)	0.044	13 (39.4)	11(28.9)	0.042
SBP, mmHg	127.3±8.9	122.4±8.3	0.047	126.3±9.3	125.1±9.9	0.067
DBP, mmHg	81.0 ±5.80	79.0±6.12	0.171	81.0±5.8	79.0±6.1	0.571
FBS, mg/dl	133.2±39.9	126.0±34.7	0.815	137.3±41.9	128.6±34.7	0.075
2HPPBS, mg/dl	168.9±59.3	158.1±43.7	0.418	173.2±69.3	159.1±42.9	0.518

p values were derived from either Chi-square test or Independent sample t test.

Both serum ALT and AST show weak and statistically insignificant correlations with systolic and diastolic blood pressure and fasting and 2 hrs postprandial blood glucose (Table IV).

Table IV Correlation of ALT and AST with other variables

Variables	ALT (IU/L)		AST (IU/L)	
	r value	p value	r value	p value
Systolic BP	0.156	0.156	0.059	0.615
Diastolic BP	0.132	0.258	0.065	0.581
FBS	0.076	0.518	0.035	0.767
2HPPBS	0.123	0.293	0.063	0.589

r: Pearson's correlation coefficient.

Discussion

NAFLD is a leading cause of liver-related morbidity and mortality.Global prevalence of NAFLD is 30%.[19] Present study was conducted to evaluate the changes of hepatic enzyme ALT and AST, in USG-diagnosed NAFLD patients. Attemps were made to observe the correlation of ALT and AST level with Systolic and Diastolic BP, FBS, 2HPPBS.

In our study, mean age of NAFLD patients were similar with subjects of previous studies.[13,20,21]

In the present study, serum ALT and AST level were elevated above the normal referral ranges, in 68% and 44% of NAFLD patients respectively, which is consistant with previous studies.[22] Mean values were also higher.A significantly greater proportion of individuals with NAFLD had elevated ALT with non significant elevation of AST in several studies.[10,11] As ALT rises more than AST, the ratio of AST to ALT not rises more than one, which was consistent with previous studies.[23,24] NAFLD with increased ALT or AST levels significantly increased the risks of cirrhosis and HCC.[25]

Diabetes mellitus is a critical determinant of NAFLD's presence and severity.[26] Forty-three percent of the patients were diabetic in the present study and both ALT and AST levels showed significant elevation in these patients. Diabetic subjects with NAFLD had significantly higher ALT, AST levels and a significantly lower AST: ALT ratio in previous study.[27] Liver enzymes, especially ALT, were independently associated with NAFLD in diabetic patients in several studies.[10,11] Few studies showed AST as being the most abnormal parameter in their diabetic populations.[28] But no relation of glycemic status (Mean FBS and 2HPPBS) of NAFLD patients were observed with the level of ALT and AST in the present study. Many diabetic patients were with medication and had lower blood glucose level. Some studies recommended that hepatic enzymes do not depend on glycemic control of NAFLD patients.[17,27,29]

The association between hypertension and NAFLD has been established in observational studies, demonstrating that each disease increases the risk of the other.[30] In the present study, elevations in ALT and AST were significantly associated with Hypertension (HTN). Serum ALT showed an independent association with hypertension in Bangladeshi adults.[31] A similar finding was observed in a previous study that reported ALT as a potential indicator of hypertension in Chinese senior adults.[32] Systolic and diastolic Blood Pressure (BP) was significantly higher in NAFLD patients. [21]

In the study, ALT was more strongly linked with systolic BP elevation than AST. In NAFLD, hepatic injury and metabolic dysfunction are strongly linked with endothelial dysfunction, arterial stiffness and RAAS activation, that predominantly elevates Systolic blood pressure rather than Diastolic blood pressure.[33]

Limitations

The present study was a time-framed cross-sectional study in a small setting with relatively smaller sample size. The diagnosis of diabetes and hypertension was partly based on reported history, which may introduce recall bias. Other potential confounding factors such as diet, physical activity, obesity indices, and lipid profiles were not fully assessed. The diagnosis of NAFLD was only based on imaging of hepatic steatosis and further fibrosis and cirrhosis were not confirmed by liver biopsy.

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Conclusion

In this study, elevated hepatic enzymes, ALT and AST in NAFLD patients were strongly associated with older age, diabetes mellitus, hypertension. Only ALT was associated with higher systolic blood pressure. Diastolic blood pressure and glycemic parameters showed no significant relationship with elevated ALT and AST. These findings highlights the need for early screening and routine monitoring of hepatic enzymes in NAFLD patients with metabolic comorbidities for early detection and management.

Recommendation

Patients with NAFLD should undergo routine monitoring of hepatic enzymes ALT and AST with regular screening for diabetes, hypertension, and cardiovascular risk factors to identify those at higher risk. Further large-scale studies are needed to strengthen these associations and guide accordingly.

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Contribution of authors

SA-Acquisition of data, data analysis, interpretation of data, drafting & final approval.

AHMS-Acquisition of data, data analysis, drafting & final approval.

SA-Conception, design, interpreetation of data, critical revision & final approval.

FT-Acquisition of data, drafting & final approval.

MB-Conception, design, critical revision & final approval.

Disclosure

The authors declared no conflicts of interest.

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