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Original Research Article

Evaluation of Liver Function Tests in Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Background: One of the most common conditions for abnormality in liver function tests is Non-alcoholic fatty liver disease (NAFLD). NAFLD is presented when more than 5% of hepatocytes become steatotic in patients who do not consume excessive alcohol consumption. Increase in this prevalence, leads to increase in the population at risk for developing chronic liver disease and its complications from NAFLD. Hence, we planned the present study to assess various liver functional tests in patients with non-alcoholic fatty liver disease.
Materials & Methods: For the present study, 317 patients were selected and various parameters for the fasting blood glucose (FBG), aspartate transaminase (AST), alanine transaminase (ALT), g-glutamyltransferase (GGT), alkaline phosphatase (ALP), triglycerides (TG), total cholesterol (TC), body mass index (BMI) and arterial blood pressure were evaluated. Determination of NAFLD was done based on the ultrasonography (USG) findings. All the subjects were divided into two groups, grade 1 and grade 2 based on the findings and grade of NAFLD. There were no patients diagnosed with grade 3 NAFLD in our study group. All the results were analyzed by SPSS software.
Results: A total of 316 male participants were included in this study. Although the levels of the liver enzymes were within the normal limits, there was a slight increasing tendency, according to the grade of NAFLD, in some of the applied tests. Significant differences were found between the age, weight, AST, ALT, GGT, ALP and BMI and the presence of NAFLD.
Conclusion: The accumulation of lipid in the liver showed by some metabolic determinants does not play a significant role in the diagnosis of NAFLD.

Key words: Liver Functional Test, Non-Alcoholic Fatty Liver.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common condition for abnormality in liver function tests because of the alarming increase in the rate obesity among population.[1] NAFLD is presented when more than 5% of hepatocytes become steatotic in patients who do not consume excessive alcohol consumption (<20 g/day for women and <30 g/day for men) and ranges in severity from simple steatosis (fat without significant hepatic inflammation or hepatocellular injury), to steatohepatitis (fat with hepatocellular injury and hepatic inflammation), through to advanced fibrosis and cirrhosis. The Third National Health and Nutrition Examination Survey (NHANES III) analyzed the data and showed the prevalence of elevated serum aminotransferases to be 7.9% in the United States, with most of the cases credited to NAFLD because these cases were unexplained.[2] The different regions of the world differ in the frequency of NAFLD and it predominates in some regions as compared to other regions. The prevalence of NAFLD in United States (US) is estimated from 16% to 23%, in Europe and in middle-east it ranges from 20% to 30%.[3,4] Obesity, one of the major risk factor for NAFLD is reaching at epidemic proportions worldwide. Increase in this prevalence, leads to increase in the population at risk for developing chronic liver disease and its complications from NAFLD.[5] Hence, we planned the present study to assess various liver functional tests in patients with non-alcoholic fatty liver disease.

MATERIALS & METHODS

This study was conducted in the Department of Biochemistry in the institution. The ethical permission for the study was obtained from the ethical committee of the institution. We selected 317 patients for the retrospective study from the patient data. A written informed consent was obtained from the patients after educating them about the procedure. Various parameters for the fasting blood glucose (FBG), aspartate transaminase (AST), alanine transaminase (ALT), g-glutamyltransferase (GGT), alkaline phosphatase (ALP), triglycerides (TG), total cholesterol (TC), body mass index (BMI) and arterial blood pressure were recorded in the subjects selected for the study. Determination of NAFLD was done based on the ultrasonography (USG) findings.

All the subjects were divided into two groups, grade 1 and grade 2 based on the findings and grade of NAFLD. There were no patients diagnosed with grade 3 NAFLD in our study group.

Patients with positive serology of hepatitis B virus and hepatitis C virus, the presence of other causes of liver disease, regular or excessive alcohol consumption (>40 gr/day), medical history which is significant for hepatic steatosis, established MS and obesity were excluded from the study. Through a retrospective review of their charts, including: age, BMI, AST, ALT, FBG, TC, TG, ALT, AST, GGT, ALP and USG results. In the assessment, NAFLD was defined as diffusely increased liver echogenicity when compared to the right kidney cortex, and graded according to the following criteria:

Grade 1: Increased diffuse echogenicity, but normal vascular walls and diaphragm echogenicity.

Grade 2: The intrahepatic vein/artery walls and diaphragm echogenicity were partly obscured by the diaphragm wall echogenicity was not visualized, and the posterior segments of the liver were poorly assessed.

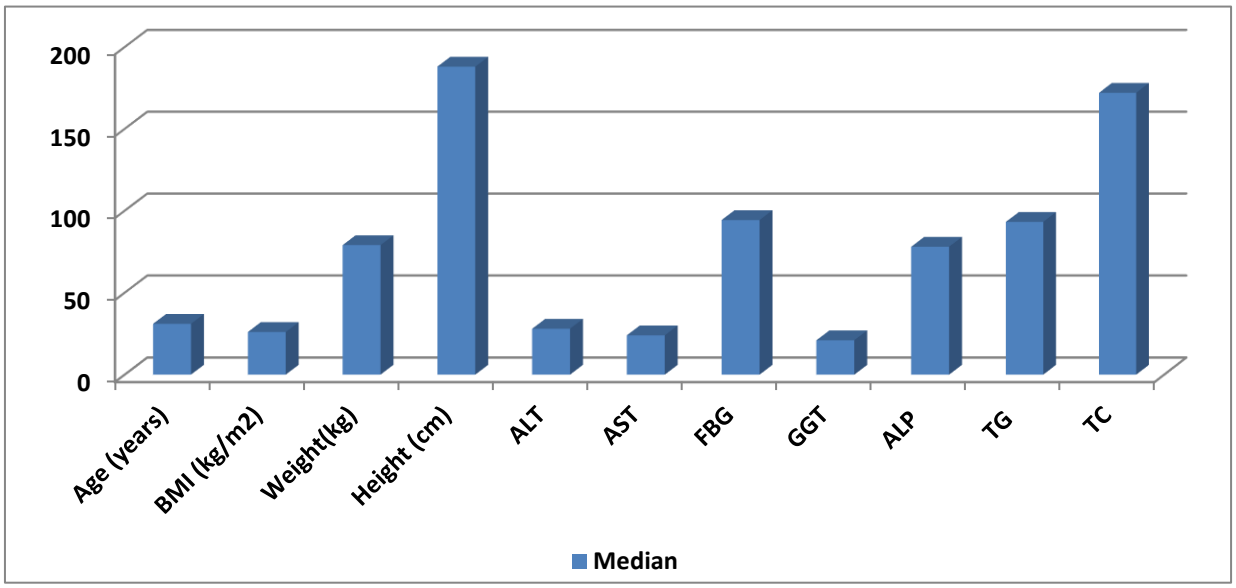
Statistical analysis

All the results were analyzed by SPSS software. Chi-square test, student t test and Mann-Whitney test were used for the assessment of level of significance. P-value of <0.05 was considered to be statistically significant.

Table 1: Biochemical test results and demographic data of subjects

Variables	Median	Min.-Max.
Age (years)	31	23-43
BMI (kg/m²)	26	19-28
Weight(kg)	79	61-98
Height (cm)	188	176-197
ALT (0-45 U/L)	28	9-45
AST (0-35 U/L)	24	14-35
FBG (74-106 mg/dl)	94.3	72-109
GGT (0-55 U/L)	21	3-57
ALP (38-155 U/L)	78	12-129
TG (50-200 mg/dl)	93.2	50-163
TC (110-200 mg/dl)	172	100-201

Figure 1: Demographic data and biochemical test results



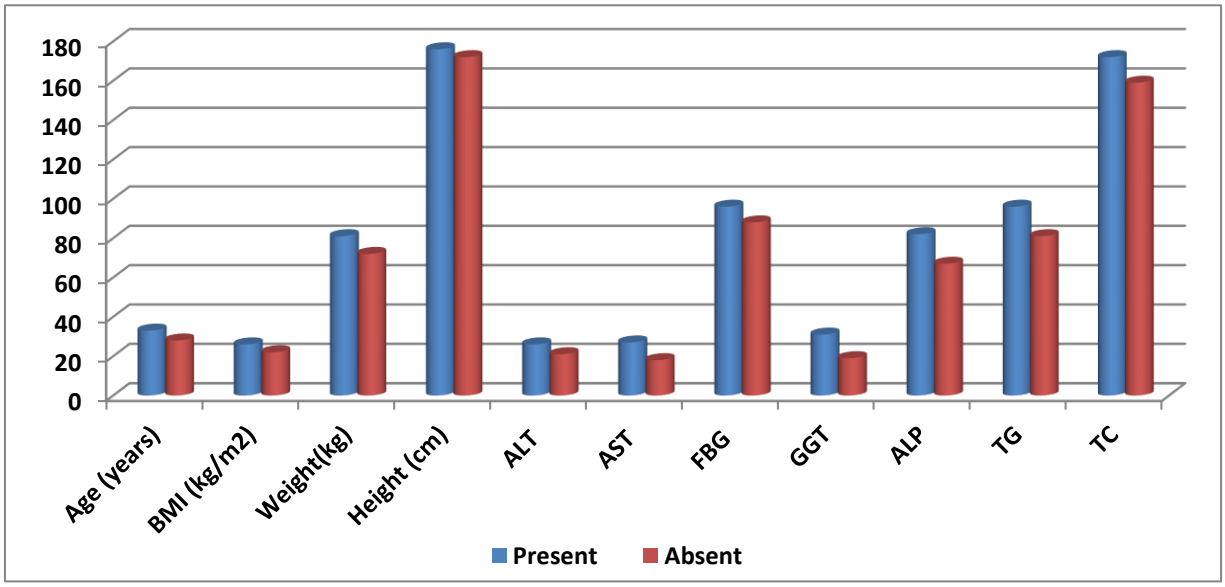
RESULTS

A total of 316 male participants were included in this study. The demographic data and biochemical test results are shown in Table 1 and figure 1, and all of the patients had normal arterial blood pressure. The USG examination revealed NAFLD in a total of 37 of the subjects; of these, 24 had grade 1 and thirteen had grade 2. There were no instances of grade 3 NAFLD found in our subjects. Although the levels of the liver enzymes were within the normal limits, there was a slight increasing tendency, according to the grade of NAFLD, in some of the applied tests. For example, the ALT, FBG, GGT, TG and TC values and the age were found to be higher in those subjects with grade 2 NAFLD than in those with grade 1 NAFLD. However, no difference was noted between the grade and the variables (Table 2). Significant differences were found between the age, weight, AST, ALT, GGT, ALP and BMI and the presence of NAFLD. ($p=0.022$, $p=0.021$, $p=0.031$, $p=0.004$, $p\leq0.001$, $p=0.003$ and $p\leq0.001$, respectively) (Table 2 and figure 2)

Table 2: Comparison of various variables between subjects with NAFLD and without NAFLD

Parameter	The presence of NAFLD		
	Present (n=37)	Absent (n=279)	P value
Age (years)	33	28	0.022
BMI (kg/m²)	26(21-28)	22(19-24)	<0.001
Weight(kg)	81(67-98)	72(57-84)	0.021
Height (cm)	176 (166-188)	172(169-185)	0.921
ALT (0-45 U/L)	26 (14-39)	21 (`11- 32)	0.004
AST (0-35 U/L)	27 (14-33)	18 (8-42)	0.031
FBG (74-106 mg/dl)	96 (81-102)	88 (75-92)	0.315
GGT (0-55 U/L)	31 (10-46)	19 (8-40)	<0.001
ALP (38-155 U/L)	82 (71-137)	67 (17-119)	0.003
TG (50-200 mg/dl)	96 (52-188)	81(50-200)	0.428
TC (110-200 mg/dl)	172(139-192)	159 (102-200)	0.431

Figure 2: Comparison of various variables between groups with NAFLD and without NAFLD



DISCUSSION

The severity of histological damage mainly determines the biological behavior of NAFLD. Presence of fatty livers only in most subjects is reported by some studies and progression to steatohepatitis or fibrosis over time is a rare condition. Some publications have reported the frequency of advanced hepatic fibrosis to be 30%–40% at the time of diagnosis, whereas well-established cirrhosis was found in 10%–15% of the patients.[6] A progression to hepatocellular carcinoma has also been emphasized in literature. Although no significant increase has been reported in the mortality rates specifically related to NAFLD, those patients with NASH usually reveal higher mortality rates (35%–85%) when compared to the overall population.[7] Hence, we planned the present study to assess various liver functional tests in patients non-alcoholic fatty liver disease.

In the present study, the prevalence of NAFLD was found to be 10.6%. However, we could not establish a comparison due to the absence of related publications on healthy young subjects. The more well-known risk factors for NAFLD are a high BMI, advanced age and the presence of MS.[8] Our study group was composed of subjects that tested negative for hepatitis, with no identified risk factors for NAFLD, but there was a significant difference with regard to the age, weight, BMI, ALT, AST, GGT and ALP in terms of the development of NAFLD, which was observed in one of ten subjects. In spite of the participants' normal hepatic enzyme levels, there was a slight tendency toward increasing, compatible with the grading of the NAFLD, in some of the applied tests. Although there could be one possible mechanism for the development of NAFLD in our subjects, due to the retrospective study design composed of healthy young subjects, we cannot establish a hypothesis for this. Furthermore, a strong correlation between NAFLD and coronary artery disease may be crucial to determining those subjects who have relevant risk factors for cardiovascular disease.[9-11] Therefore; USG can be applied as a screening tool along with routine check-ups.

Armstrong et al conducted a study to calculate the range of disease severity of NAFLD in a primary care setting. Adult patients with incidental abnormal LFTs, in the absence of a previous history, or current symptoms/signs of liver disease were prospectively recruited from eight primary care practices in Birmingham. NAFLD was diagnosed as fatty liver on ultrasound, negative serological liver aetiology screen, and alcohol consumption30 and20 g/day in males and females, respectively. The NAFLD Fibrosis Score (NFS) was calculated to determine the

presence or absence of advanced liver fibrosis in subjects identified with NAFLD. Data from 1118 adult patients were analyzed. The cause of abnormal LFTs was identified in 55% of subjects, with NAFLD and alcohol excess accounting for the majority. A high NFS suggesting the presence of advanced liver fibrosis was found in 7.6% of NAFLD subjects, whereas 57.2% of NAFLD patients had a low NFS allowing advanced fibrosis to be confidently excluded.[12] Giovanni Musso et al. assessed the evidence in: (1) natural history of NAFLD; and (2) non-invasive methods to differentiate NAFLD histological subtypes. Among 4185 articles published on MEDLINE, Cochrane Library, EMBASE, Pubmed, national and International meeting abstracts through 2010, 40 articles assessing the natural history of NAFLD and 32 articles evaluating the diagnostic accuracy of non-invasive tests against liver biopsy (LB) were included. Two reviewers retrieved articles and evaluated study quality by appropriate scores. Main outcomes were pooled using random- or fixed-effects models. NAFLD had an increased overall mortality, deriving from liver-related and cardiovascular disease, and a 2-fold risk of diabetes. Compared to SS, NASH has a higher liver-related, but not cardiovascular mortality. Three non-invasive methods received independent validation: pooled AUROC, sensitivity and specificity of cytokeratin-18 for NASH are 0.82, 0.78, and 0.87. For NASH with advanced fibrosis, pooled AUROC, sensitivity and specificity of NAFLD fibrosis score and Fibroscan are 0.85, 0.90, 0.97 and 0.94, 0.94 and 0.95.[13]

Gokcan Okur et al. determined prevalence of non-alcoholic fatty liver disease (NAFLD) in healthy young person's admitted for annual medical check-ups. A retrospective study was conducted in a military hospital. Total of 254 healthy males were included and participants were divided into 2 groups according to presence and grade of NAFLD. Demographic data, biochemical test results, and ultrasonography findings were collected from all patients. Statistical analyses were performed using SPSS software, version 22.0 (SPSS, Inc., Chicago, IL, USA).Prevalence of NAFLD was 10.6%. Significant differences were found with regard to age; levels aspartate transaminase, alanine transaminase, gamma-glutamyltransferase, and alkaline phosphatase; body mass index (BMI); and presence of NAFLD. When compared to those with grade 1 NAFLD, levels of alanine transaminase, fasting blood glucose, gamma-glutamyltransferase, triglycerides, total cholesterol and age variables were higher in those with grade 2 NAFLD. However, no statistically significant difference was noted when comparing grades of NAFLD. Though this study included patients with normal BMI and normal laboratory test results, presence of NAFLD was not rare in these otherwise healthy young men. Liver enzyme levels were within normal limits; however, there was slight tendency to be high consistent with presence and grade of NAFLD.[14]

CONCLUSION

From the above results, the authors concluded that the accumulation of lipid in the liver showed by some metabolic determinants does not play a significant role in the diagnosis of NAFLD.

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