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ASSOCIATION OF NON-ALCOHOLIC FATTY LIVER DISEASE WITH HEPATIC ENZYMES AMONG ADULT POPULATION OF NORTH INDIA

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is a common clinical condition which is fast assuming importance as a possible precursor of more serious liver disorders, including cirrhosis of the liver and hepatocellular carcinoma. The present study was performed to assess the association of NAFLD with hepatic enzymes among north Indian subjects. A sample of 76 subjects was taken for the present case-control study. For each case two healthy volunteers (age±3 years & gender matched) were selected. Study subjects includes patients who underwent USG examination of any part of the body and asymptomatic, apparently healthy attendants accompanying the patients were subjected to abdominal USG examination, individuals who gave a history of alcohol abuse were excluded from the study. Hepatic function tests included alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and serum bilirubin total were performed by standard laboratory procedures. Appropriate statistical methods were used for data analysis. The ALT was observed to be significantly ($p<0.0001$) higher among the subjects of NAFLD (42.55±16.02) as compared to controls (30.75±7.41). Similarly, AST (NAFLD=35.92±14.90, Controls=32.43±8.09; $p=0.01$) and ALP (NAFLD=271.97±66.23, Controls=141.36±49.95; $p<0.0001$) were also found to be significantly higher among NAFLD subjects as compared to controls. Whereas, no significant difference was seen in serum bilirubin total levels (NAFLD=0.92±0.16, Controls=0.89±0.20; $p=0.15$) among both groups. Conversely, results of multivariate logistic regression analysis shown that ALT (OR=2.34, 95%CI=1.12-4.56; $p=0.03$) and ALP (OR=1.03, 95%CI=10.02-1.04; $p=0.04$) were found to be significant risk factors for NAFLD. Hence it can be concluded that elevated ALT and ALP were the risk for NAFLD.

KEY WORDS: Nonalcoholic fatty liver disease, ultrasonography, hepatic function test, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, serum bilirubin total

INTRODUCTION

NAFLD is a clinicopathological condition characterized by significant lipid deposition, usually greater than five percent of the liver weight deposited as triglyceride, in the patient's liver parenchyma, without history of excessive alcohol consumption (1,2). Although hepatic steatosis is the most common presentation, the spectrum of NAFLD varies greatly from steatosis to nonalcoholic steatohepatitis, fibrosis or cirrhosis (3,4). NAFLD is reported to be related to obesity, diabetes mellitus (DM), or hyperlipidemia (5-8) However, NAFLD still may occur in lean persons who otherwise appear healthy and do not seek medical consultation for symptoms (1,7). NAFLD is considered the most common liver disease in the Western population; its prevalence ranges from 20-30 percent (9). The prevalence of NAFLD in the Eastern population is about 10 percent, but it may be increasing because of increasing westernization of dietary habits, less physical activity, and increasing incidence of obesity (9-11). NAFLD is one of the most common causes of chronic elevation of hepatic enzymes in the general population. This clinicopathological syndrome has been increasingly recognized as a major cause of liver-related morbidity and mortality (12). There is no data in the published in literature on the correlation of NAFLD with hepatic enzymes among north Indian adult population.

The present study was undertaken to demonstrate whether there is a relationship between the presence of NAFLD and extent of elevated hepatic enzymes among north Indian adult population.

MATERIAL AND METHOD

Case-control study design was used for data collection in present study. This study has been done in Northern part of India at Department of Radiodiagnosis, King George's Medical University, Lucknow. A total 76 subjects were selected by purposive sampling method. For

each case (NAFLD), two healthy controls as volunteers were chosen by age (±3years) and gender matched. Study sample embraces patients aged between 20-60 years, who underwent USG examination of any part of the body and asymptomatic and apparently healthy attendants. Individuals with any of the following were excluded from the study: History of alcohol consumption, presence of HBsAg or anti-HCV antibodies, fatty liver suspected to be secondary to hepatotoxic drugs, inflammatory bowel disease, prior surgery that could cause fatty liver, or celiac disease. Pregnant and lactating women were also excluded. Fatty liver was diagnosed by abdominal USG (upper abdomen) using standardized criteria (13).Venous blood was drawn in the morning after an overnight fast. Hepatic function tests incorporated ALT, AST, ALP and serum bilirubin were determined by standard laboratory procedures in the same laboratory by standard laboratory methods recommended by International Federation Clinical Chemistry. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institution's Human Research Committee. All study participants signed informed consent before sample collection. Continuous variables are presented as means±SD. To test differences in continuous variables between the two groups, the independent samples t-test (for normally distributed variables) was used. The multivariate logistic regression analysis (matched method) was carried out to find the significant factors associated with NAFLD. A value of p <0.05 was considered statistically significant. All the analysis was carried out by using SPSS 16.0 version.

RESULT

A total of 76 consecutive patients with NAFLD diagnosed through compatible ultrasonography in the absence of known etiologies of liver disease (in all subjects). 152 healthy volunteers were selected as controls by age (±3 years) and gender matched to assess the correlation between NAFLD and hepatic enzymes. Mean age of NAFLD 46.22±10.38 and controls 45.33±12.27. More than half numbers of subjects were reside in urban area (NAFLD= 61.8%, controls= 56.6%). The higher percent of subjects were belong to Hindu religion (NAFLD= 77.6%, controls=73.0%) whereas, only 22.4% and 27.0% subjects belongs to Muslim religion NAFLD and controls respectively.

Table 1 showed that the increased level of ALT (42.55±16.02) was observed among NAFLD subjects when compared with controls (30.75±7.41). The difference in the level of ALT between NAFLD subjects and controls was found to be highly significant (p<0.0001). However, AST was also significantly (p=0.01) higher among the subjects of NAFLD (35.92±14.90) than controls (32.43±8.09). A highly significant (p<0.0001) difference was found in the level of ALP among NAFLD (271.97±66.23) than control (141.36±49.95) subjects. Contrary to this, the serum bilirubin total level was 0.92±0.16 among NAFLD subjects and 0.89±0.20 among controls, the difference was found to be statistically non-significant (p=0.15).

Table 1: Association of NAFLD with hepatic function test

Hepatic Function Test	NAFLD (n=76)	Controls (n=152)	t and p-value,
	Mean±SD	Mean±SD	
ALT	42.55±16.02	30.75±7.41	3.61, <0.0001*
AST	35.92±14.90	32.43±8.09	2.56, 0.01*
ALP	271.97±66.23	141.36±49.95	16.63, <0.0001*
Serum bilirubin	0.92±0.16	0.89±0.20	1.84, 0.15

*Significant

Table 2 showed that the significant risk factors for NAFLD (among various hepatic enzymes) were evaluated by using multivariate logistic regression analysis. The Hepatic enzymes found to be significant in the bivariate analysis were then entered in the backward logistic regression model to find out the significant risk factor for NAFLD (among hepatic enzymes). Separate models were evaluated for different groups of factors. The risk of NAFLD was higher among those subjects whom ALT (OR=2.34, 95%CI=1.12-4.56; p=0.03) and ALP (OR=1.03, 95%CI=10.02-1.04; p=0.04) levels were detected higher.

Table 2: Significant risk factors for NAFLD-Multivariate logistic regression

Significant Factors	OR	95.0% C.I. for OR		p-value
		Lower	Upper	
ALT	2.34	1.12	4.56	0.03*
ALP	1.03	1.02	1.04	0.04*

*Significant

DISCUSSION

NAFLD is a common referral to Gastroenterologists and Hepatologists (14). The diagnosis is suspected in patients with elevated aminotransferases. In some patients with NAFLD, the diagnosis is suspected in the presence of even mildly elevated aminotransferases (15). Although 80 percent of patients with steatosis may have aminotransferases in the normal range (15), ALT and AST fluctuate, with two-thirds of patients with NASH having normal levels at any point in time (16,17). ALP may also be mildly elevated. However, Hyperbilirubinemia indicate a state of advanced liver disease and is not otherwise found in NAFLD (18).

In the present study ALT was found significantly higher among cases than controls (NAFLD=42.55±16.02, controls=30.75±7.41; p<0.0001) similarly, a study conducted by Rodríguez-Hernández et al. (2008) in Mexico reported that the ALT (54.4±33.3 and 39.8±29.8; p=0.03) was increased significantly higher in NAFLD subjects (19). On the other hand, Nigam et al. (2013) also reported that, significantly higher values of ALT (NAFLD 36.15±22.69, controls 30.16±11.42; p=0.005) was recorded among NAFLD subjects (20). AST was found to be higher among NAFLD (35.92±14.90) than controls (32.43±8.09) which was statistically significant (p=0.01). Likewise, in another study AST (NAFLD 41.58±31.52, controls 32.90±18.57; p=0.005) was recorded significantly higher values among NAFLD than in controls (20). A highly significant (p<0.0001) values of ALP was observed among NAFLD subjects than controls. Previous report showed that, serum level of ALP was elevated in 30 percent of patients (21). However, in the current study serum bilirubin (total) level of was non-significantly associated with NAFLD. A study conducted on middle aged Korean worker by Chang et al. (2012) described the same findings that serum bilirubin (total) level was not significantly associated with incidence of NAFLD (22).

In the present study results of multivariate regression analysis showed that ALT was a significantly associated with NAFLD (OR=2.34, 95%CI=1.12-4.56; p=0.03). Rodríguez-Hernández et al. (2008) also originate the same observations among NAFLD and ALT (OR 2.7; 95% CI, 1.3-10.4, P<0.001) (19). In the same way, the risk factor significantly (OR, 15.45; 95% CI, 8.21-29.09, P<0.001) associated with NAFLD was elevated ALT (23). ALP was also found a significant risk factor for NAFLD (OR=1.03, 95%CI=10.02-1.04; p=0.04) correspondingly, Chen CH et al. (2006) also reported that elevated ALP was significantly associated with NAFLD (OR 1.67 95%CI, 1.32-2.13, P<0.05) (23).

CONCLUSION

The development of NAFLD is closely associated with elevated ALT and ALP among adult population of North India.

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