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PREVALENCE OF NASH IN NAFLD PATIENTS WITH RAISED HEPATIC ENZYME LEVELS

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ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) has been considered a benign condition related to obesity and with metabolic syndrome. It is a chronic condition ranging from simple steatosis (hepatic triglyceride accumulation more than 5.5% in MRI or more than 5% corresponding 250 mg program by wet weight) up to hepatic carcinoma. **Material & Methods:** The present single Centre observational study was conducted by following all protocols of ethical conduct including written and informed consents of the patients. Confirmed patients of NAFLD by ultra-sonography (USG) who were visiting outpatient department of our hospital were enrolled in our study. The study was conducted in Department of Biochemistry in association with Department of Gastrologer & Endocrinology. **Results:** Serum ALT, AST levels were also significantly higher in the diabetic NAFLD patients. Serum ALT levels were significantly more elevated than serum AST levels. For the pre diabetic group mean level of AST (U/L) was 33.08 ± 13.35 and for the diabetic group mean level of AST (U/L) was 47.72 ± 46.70 (t value = -3.014; P=0.003). Similarly, for the pre diabetic group mean level of ALT (U/L) was 48.37 ± 20.63 and for the diabetic group mean level of ALT (U/L) was 77.72 ± 72.99 (t value = -3.870; P=0.000). It was reported that Serum ALT, AST levels were also significantly higher in the diabetic NAFLD patients. **Conclusion:** By help of clinical findings and with can biochemical markers, we can screen NAFLD early and almost all centers. Early diagnosis of NAFLD helps patients to improve their condition with NAFLD by daily exercises and with Lifestyle changes and the prognosis would be better.

Key words: NAFLD, Hepatic enzyme, AST, ALT, NASH.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has been considered a benign condition related to obesity and with metabolic syndrome. It is a chronic condition ranging from simple steatosis (hepatic triglyceride accumulation more than 5.5% in MRI or more than 5% corresponding 250 mg program by wet weight) up to hepatic carcinoma **(1)**. Most people with NAFLD are asymptomatic. There is accumulation of fat in liver but no inflammation or liver damage is observed. Such a condition termed as fatty liver. In severe conditions, it may develop in to non-alcoholic steatohepatitis (NASH), cirrhosis and hepatocellular

carcinoma in which the liver is permanently damage and no longer able to work properly **(2)**.

Many patients with NAFLD will be overweight or obese but asymptomatic and have normal liver function tests (LFT). NAFLD is typically first suspected when the result of LFT are moderately abnormal **(3)**. The common presentation of NAFLD is moderately abnormal liver function test. Raised transaminase levels (ALT and AST) along with insulin resistance or type 2 Diabetes mellitus, impaired lipid profile, high or normal HbA1c are strongly suggestive of NAFLD or hepatic steatosis with fatty liver confirmed by USG in absence alcohol consumption **(4)**.

Clinical and pathological studies demonstrate that NAFLD is an important source of unexplained rise in hepatic transaminases, cryptogenic cirrhosis and cryptogenic hepatocellular carcinoma in Indian patients **(5)**. The fact that oxidative stress is involved in the pathogenesis of NAFLD/NASH but no roll found with serum or liver iron and HFE gene in Indian patients **(6)**. Imaging modalities are not useful in differentiating simple steatosis from NASH and liver biopsy may be helpful in those with risk factors for significant liver disease **(7)**. Hence, we conducted present study to evaluate the prevalence of NASH in NAFLD patients with raised hepatic enzyme levels.

MATERIALS & METHODS

The present single Centre observational study was conducted at Mahatma Gandhi Medical College and Hospital, Jaipur. The study was conducted in Department of Biochemistry in association with Department of Gastrologer & Endocrinology. The study was conducted in duration of one year, after seeking approval from the Institutional Ethics Committee. All protocols of ethical conduct including written and informed consents of the patients enrolled for the study was strictly complied. Confirmed patients of NAFLD by ultra-sonography (USG) who were visiting outpatient department of our hospital were enrolled in our study. Calculated Sample size of study was 200 and patients were equally enrolled in prediabetic and diabetic group. Detailed socio-demographic data were taken and recorded along with general physical and clinical examination. Inclusion criteria for the patients includes adults i.e. > 18-60 years of age and patients who had elevated serum ALT & AST > 2 to reference values. Patient who were alcoholic, pregnant and lactating mothers, patient with other forms of chronic liver disease such as viral or autoimmune hepatitis, medication induced liver disease, patients who had bariatric surgery, any kind of active or recent malignancy, patients on medication associated with fatty liver disease were excluded from the study. The patients selected on the basis of above defined criteria was further subjected to investigations; Aspartate transaminase (AST), Alanine transaminase (ALT) by Kinetic with pyridoxal 5 phosphate, Serum Lipid Profile, Cholesterol by Enzymatic (CHO-POD) method, Triglycerides (TG) by Enzymatic (GPO/POD) method, High Density Lipids (HDL-Chol) by Phosphotungstic Acid/MgCl2-Enzymatic method, Low Density Lipids (LDL) and Very Low Density Lipids (VLDL) shall be calculated by Friedewald formula i.e. VLDL = TG/5 and LDL= Cholesterol – (HDL+VLDL), Insulin by CMIA, Homeostatic model assessment- Insulin resistance (HOMA-IR), Viral Markers- HbsAg, Anti HCV and HIV. The results thus obtained shall be subjected to statistical analysis. The data were analyzed by using software's MS Excel 2010, Epi Info v7 and SPSS v22.

RESULTS

Total 200 patients were enrolled for the study. Out of them 100 patients were selected in diabetic group and 100 patients were selected in pre-diabetic group. Serum levels of ALT and AST were estimated in the Enrolled patients were presented as mean and SD For the pre diabetic and diabetic groups. All the analytes were compared by applying student t-test. The mean age of subjects of both groups was comparable. For the pre diabetic group mean level of AST (U/L) was 33.08 ± 13.35 and for the diabetic group mean level of AST (U/L) was 47.72 ± 46.70 (t value = -3.014; P=0.003). Similarly, for the pre diabetic group mean level of ALT (U/L) was 48.37 ± 20.63 and for the diabetic group mean level of ALT (U/L) was 77.72 ± 72.99 (t value = -3.870; P=0.000). It was reported that Serum ALT, AST levels were also significantly higher in the diabetic NAFLD patients. Serum ALT

levels were significantly more elevated than serum AST levels. (Table 1)

Table 1: Hepatic enzyme levels in pre-diabetic and diabetic patients of NAFLD

Parameters	Mean ± SD		t-value	P value
	Pre DM	DM		
AST (U/L)	33.08 ± 13.35	47.72 ± 46.70	-3.014	0.003
ALT (U/L)	48.37 ± 20.63	77.72 ± 72.99	-3.870	0.000

In the present study the prevalence of NASH is in Association with the serum AST levels positively affect the occurrence of NASH and it was found statistically highly significant by applying Chi square test (x2 = 32.662; P=0.000). (Table 2)

In the present study, the prevalence of NASH is in Association with the serum ALT levels positively affect the occurrence of NASH and it was found statistically highly significant by applying Chi square test (x2 = 39.799; P=0.000). (Table 3)

Table 2: Prevalence of NASH in NAFLD patients with AST

Groups	Sub-groups		Chi-square	P-Value
	AST <2 No. (%)	AST >2 No. (%)		
NASH	26 (68)	12 (32)	32.662	0.000
No NASH	161 (99)	01 (1)		

Table 3: Prevalence of NASH in NAFLD patients with ALT

Groups	Sub-groups		Chi-square	P-Value
	ALT < 2 No. (%)	ALT > 2 No. (%)		
NASH	24 (63)	14 (37)	39.799	0.000
No NASH	161 (99)	01 (1)		

DISCUSSION

NAFLD refers to a group of disorder including asymptomatic conditions like liver cirrhosis to more severe condition like NASH, which present with progressive apoptosis and Fibrosis. NASH was first define by Ludwig et al in 1980 as a condition presenting with inflammatory changes liver function test **(8)**. Since then liver biopsy has remained the method of choice for diagnosis as well as evolution of the degree of necrotic inflammation of liver tissue in NASH. In an epidemiological study by El serag HB et al., 2004 two to three times increased risk of future end stage Liver disease and hepatocellular carcinoma was reported in Diabetic patients **(9)**.

All the biomarkers estimated in the Enrolled patients were presented as mean ± SD For the pre diabetic and diabetic groups. All the analytes were compared by applying student t-test the major observations reported that the mean age of subjects can both groups was comparable and Serum ALT, AST levels were also significantly higher in the diabetic NAFLD patients. Serum ALT levels were significantly more elevated than serum AST levels. Of the total 200 NAFLD patients enrolled for the study 38 (16%) confirmed for NASH. The significance of elevated AST and ALT level in patients of NAFLD with NASH was further explore in the study on applying Chi square test it was observed that Serum AST and ALT level more than 2 Times the upper normal limits have a highly significant Association with occurrence of NASH **(10)**.

In the present study, Serum levels of ALT and AST were estimated in the Enrolled patients were presented as mean and SD For the pre diabetic and diabetic groups. All the analytes were compared by applying student t-test. The mean age of subjects of both groups was comparable. For the pre diabetic group mean level of AST (U/L) was 33.08 ± 13.35 and for the diabetic group mean level of AST (U/L) was 47.72 ± 46.70 (t value = -3.014; P=0.003). Similarly, for the pre diabetic group mean level of ALT (U/L) was 48.37 ± 20.63 and for the diabetic group mean level of ALT (U/L) was 77.72 ± 72.99 (t value = -3.870; P=0.000). In fact out of the 162 patients with known as like manifestations only one patient 0.6% presented with serum aspartate transaminase and alanine transaminase level more than twice the normal values. The study therefore

proposes that aspartate transaminase and alanine transaminase level above 2 times the upper normal range should be identified as a risk factor for development of NASH **(11)**.

In the present study the prevalence of NASH is in Association with the serum AST levels positively affect the occurrence of NASH and it was found statistically highly significant by applying Chi square test (x2 = 32.662; P=0.000). In the present study, the prevalence of NASH is in Association with the serum ALT levels positively affect the occurrence of NASH and it was found statistically highly significant by applying Chi square test (x2 = 39.799; P=0.000). In a review by Elizabeth H and Harish MD et al., 2005 it was concluded that type 2 Diabetes mellitus patients commonly present with abnormal liver function test the study suggests that insulin resistance in manifested by mild increase in the transaminases level. It suggests that administration of antidiabetic drugs tend to decrease alanine transaminase levels **(12)**.

CONCLUSION

We concluded from the present study that diabetes patients are at high risk to develop NAFLD or worse condition like elevated liver enzymes or cirrhosis or even hepatic carcinomas and Have poor prognosis. Liver biopsy test diagnosis of choice in case of NAFLD to Differentiate hepatic ballooning due to NAFLD or any other hepatic pathology like infections or overuse of drugs. By help of clinical findings and with can biochemical markers, we can screen NAFLD early and almost all centers. Early diagnosis of NAFLD helps patients to improve their condition with NAFLD by daily exercises and with Lifestyle changes and the prognosis would be better.

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