Original article:

Alarming high levels of transaminases in non insulin dependent diabetes mellitus

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Abstract:

Objective: The liver plays a major role in pathogenesis of type2 Diabetes. Moderately increased liver markers are found in type2 Diabetes. This study was to determine the prevalence of increased liver enzymes in subjects with consistent Hyperglycemia and Hyperlipidemia.

Material and Method: A study of 650 subjects was done out of which 400 were suffering from type2 Diabetes age 40-60 years and 200 were healthy control subjects.

Results: Liver enzymatic markers abnormalities were found in 350. Out of these 50 had a previous history of alcohol abuse. These patients were included in the study. Elevations in serum ALT,AST, Alkaline Phosphatase were found in 300 patients. Serum total cholesterol, TG, LDL were also found elevated in patients with abnormal liver function test when compared with normal healthy control group.

Conclusion: Alanine Transaminase the most important liver enzymatic marker is associated majority with type2 Diabetes and with Hyperlipidemia.

Keywords : Non alcoholic fatty liver disease, Liver function tests

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Introduction: Liver function tests(LFTS) are commonly used in clinical practice to cure the liver disease, monitor the progression of known disease and monitor the effects of potentially hepatotoxic drugs [1]. Individuals with type2 have a higher incidence of liver function abnormalities than those who do not have Diabetes. Chronic elevations of transaminases often reflect underlying insulin resistance [2].Few studies have shown that markers of liver injury can independently predict type2 Diabetes mellitus [3].Hepatotoxicity is a known complication of statin therapy especially in those treated with high doses and if used in combination with a filtrate. Routine LFT monitoring in this situation is a common practice.Oral ant-diabetic agents such as Sulphonylimeas, Thiazolidinedione and Alpha-glycosidase inhibitors may also cause hepatic injury with resultant LFT derangements [4-7]. Deranged liver enzymes related to poor Diabetes control have also been described [8].Mild chronic elevation of transaminases often reflects underlying insulin resistance [9]. Also of significance is the high frequency of transaminase abnormalities in obese patients with type2 Diabetes. This probably reflects the strong association between Obesity and NAFLD.Insulin resistance is the common factor. With the world wide prevalence of obesity on the rise, the incidence of Diabetes is also expected to

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escalate and presumably LFT abnormalities will be more commonly encountered in Diabetes clinics[10]. The purpose of this study was to determine the prevalence of asymptomatic LFT abnormalities in Indian population with type2 Diabetes Mellitus, attending SBRM Hospital of Lovely Professional University.

Material and Methods: The study was a retrospective study of patients with type2 Diabetes mellitus attending the SBRM Hospital. For each subject, clinical findings and laboratory results were recorded including age, gender and duration of diabetes. The past medical History was reviewed to explain abnormal LFT's. Anthropometric data included height and body mass for calculation of body mass index (BMI) weight (Kg) and height (m2)[11]. Patients were categorized according to the following BMI groups for comparison: Normal weight: (BMI < 25 Kg/m2),Overweight & obese (BMI > 25 Kg/m2),Obese (BMI ≥ 30 kg/m2) and morbidity obese (BMI ≥ 40 Kg/m2).The following laboratory tests were recorded: Liver function tests (Serum ALP (alkaline phosphatase), ALT (Alanine transaminase), AST, Serum Lipids (Total cholesterol, HDL cholesterol, LDL cholesterol, Total triglycerides) . Standard span kits were used for the estimations. Liver enzymes were defined as abnormal if the concentration exceeded the upper limit of normal (ULN) for the reference range. The prevalence of the abnormal Liver enzymes (ALE) was calculated in total study group. Patients with a history of alcohol abuse or liver disease including those with a past medical history were excluded from further analysis. The remaining subjects were stratified according to gender and BMI category. Data is presented as Mean ±, Standard deviation (SD) or as a percentage (%). A P- Value <0.01 was considered significant.

Table No.1: Showing different variables in subjects of diabetes with and without fatty liver

Values are Mean ± SD (P<0.001) highly significant.

P<0.01 moderately significant, n=4

VARIABLES	Without fatty liver	With NAFLD	P-Value
N	100	350	
Sex (% men)	54	56	< 0.001
Age (years)	60±3	62±6	< 0.001
BMI (Kg/m^2)	26.5±2	28.3±4	< 0.001
Diabetes duration (years)	7±2	12±3	< 0.001
Systolic BP (mmHg)	135±10	138±12	< 0.001
Diastolic BP (mmHg)	83±7	85±10	< 0.001
Fasting Glucose (mg/dl)	106.6±9.0	180±12.0	< 0.01
Triglycerides (mmol/L)	1.40±0.6	1.68±1.0	< 0.001
HDL Cholesterol (mmol/L)	1.41±0.3	1.34±0.4	< 0.001
LDL Cholesterol (mmol/L)	1.40±0.4	3.37±0.4	< 0.001
AST(U/L)	23±3	28±10	< 0.001
ALT(U/L)	25±3	33±12	< 0.001
ALP(U/L)	36 +_5	47+_7	<0.001

Discussion: Out of 450 subjects and 200 controls, 100 subjects were found without fatty liver on ultra sound and normal liver enzymes and 350 with fatty liver and abnormal liver markers. All the results are shown in table 1. Our study showed that in Diabetic patients with duration >12 years and fatty liver, the elevation of triglycerides is highly significant as compared to Diabetes without Fatty liver. (P<0.001). This may be due to fatty acids in the liver coming from different sources: Derived from dietary fat, released from adipocytes via lipolysis and from non-hepatitis lipogenesis. An imbalance of any of the pathway involved in tri-acyl glycerol delivery, synthesis, export or oxidation could contribute to its accumulation in the liver[12].Estimation of HDL-Cholesterol is useful to identify the effect of hyperglycemia on liver because HDL acts as a scavenger to decrease the accumulation of bad cholesterol in the arteries (LDL).The levels of HDL-cholesterol when compared between NAFLD subjects and Non NAFLD was found to have a very significant decrease (P<0.001).This may be due to the

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strong association between NAFLD and type 2 Diabetes and the prevalence of both disorders is increasingly related to an increase in the prevalence of obesity and insulin resistance[13-14].Increase in LDL (Bad cholesterol is also significant (P<0.001) as compared to non NAFLD patients may be due to visceral obesity and hepatic fat correlate with insulin resistance which is an important precision to development of type2 Diabetes and secondary to increased tumor necrosis factor(TNF), α and direct or Autoimmune damage to β-cells by the viruses[15-16].The level of liver enzymes (AST&ALT) were also found to be significantly increased (P<0.001) in comparison with patients without fatty liver due to decreased plasma levels of adiponectin, an adipose secreted cytokine with anti-atherogeninc properties[17]may represent another possible mechanism linking NAFLD and increase in lipids.This was also validated by a study of Hui etal[18]

Also study concludes that adiponectin has anti-inflammatory properties in the liver and its deficiency might account for high amino transferase and liver disease progression. NAFLD is a common liver disorder that is strongly associated with insulin resistance and type2 Diabetes. With the increase in number of individuals who are overweight or obese, this condition will only increase in prevalence. The mechanism underlying the development of NAFLD are not completely understood but likely involve a combination of increased FFAs and possibly decreased Lipid oxidation in the liver as a result of insulin resistance. We found that markers of liver injury ALT and AST were significantly associated with risk of incident type2 Diabetes. These findings suggest that NAFLD or related pathologies may predispose to type2 Diabetes. Future research should focus on classifying the relationship between hepatic and peripheral insulin resistance and the development of liver disorders. Routine monitoring of LFTs in patients with type 2 Diabetes should occur at the start of drug therapy and if patients develop symptoms raising concern about hepatic impairment awareness by health care providers is essential for early diagnosis and timely implementation of life style and pharmacological interventions.

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