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Original Research Article

A Case-Control Study of Lipid Profile and Liver Enzymes in Type-II Diabetes Mellitus at SMS Medical College & Attached Hospitals Jaipur (Rajasthan)

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Conflict of interest: Nil

Abstract

Background: Type 2 DM has been linked with dyslipidemia and elevation of some liver enzymes; in fact, it has been identified as independent risk factor for development of coronary artery disease (CHD). The liver helps to maintain normal blood glucose concentration in the system. This function is deranged in association with liver enzymes abnormality in type 2 DM and in obese individuals. It helps to predict any form of metabolic insult to the liver. The present work was designed to estimate the lipid profile and liver enzymes and to find the association between them in type 2 diabetes patients.

Materials & Methods: After taking necessary permissions, a cross sectional study was conducted at Department of Biochemistry and Department of Endocrinology / Medicine, SMS Hospital, Jaipur. This study includes 30 patients suffering from type 2 diabetes aged 40-70 years compared with 30 controls. Samples were analyzed for the measurement of serum glucose, lipid Profile and Liver function tests by Colorimetric method and HbA1C measured by latex turbidimetric method.

Results: Results were analyzed statistically by Student's t-test and Pearson correlation coefficient test. Both Lipid Profile and Liver function tests were significantly elevated in patients as compared to controls. There was statistically highly significant positive correlation between Lipid Profile levels with GGT and Alkaline Phosphatase in diabetic patients.

Conclusion: This study suggests routine monitoring of the commonly used lipid parameters (especially TG, TC and HDL-C) and LFT among patients with T2DM is warranted in our population which could be considered to be the epi-center for T2DM or CAD. Early recognition and appropriate treatment of significant postprandial dyslipidemia and altered LFT's is of paramount importance in diabetics so as to reduce impending complications.

Keywords: Diabetes Mellitus (DM), Glycated haemoglobin(HbA1c), Lipid Profile, LFT.

Introduction

Type 2 Diabetes Mellitus (T2DM) is an endocrine disorder. It is characterized by high levels of glucose in the blood resulting from variable degrees of insulin resistance and deficiency. Chronic hyperglycemia can lead to multi-organ damage resulting in

many complications on the renal, neurologic, and cardiovascular systems and many disturbances in carbohydrate, lipid, protein metabolism.[1-3] The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues.

Diabetes is one of the largest global health emergencies of this century, ranking among the 10 leading causes of mortality together with cardiovascular disease (CVD), respiratory disease, and cancer.[4] Diabetes mellitus as ruling cause of death worldwide is one of the most severe health problems in 21st century.[5] It is estimation that, more than 360 million individuals may develop diabetes by the year 2030.[6] Diabetes has steadily increased in India and around the world over the last three decades, with India accounting for a sizable portion of the global burden. The estimates in 2019 showed that 77 million individuals had diabetes in India, which is expected to rise to over 134 million by 2045. Approximately 57% of these individuals remain undiagnosed.[7]

It is well known that the liver is a vital organ in the metabolism of carbohydrates and in maintaining glucose homeostasis during fasting and postprandial period.[8] ALT has been considered the specific marker of liver injury, as found in high concentrations in hepatocytes[9], while GGT is present on the surface of most cell types and highly active in the liver, kidneys, and pancreas.[10] Also, GGT is responsible for extracellular glutathione catabolism and may be linked to oxidative stress[11] and chronic inflammation[12]; both oxidative stress and chronic inflammation are important pathways for hepatic insulin resistance (IR) and subsequently T2D development.[13]

Hyperinsulinemia and IR play an important role in lipid abnormalities for T2D patients.[8] Diabetic dyslipidemia is initiated by the elevation of Triglyceride (TG) rich Very Low Density Lipoprotein (VLDL-C) from hepatic overproduction. Although dyslipidemia affects the major organ systems, the liver is considered to be highly affected due to its close association in lipid metabolism. The liver plays a significant role in lipid metabolism by manufacturing, storing, and transporting lipid metabolites.[14]

As there were less published studies done locally on liver enzymes and lipid profiles in T2DM patients, this study was conducted to determine the association of Liver Function Tests (LFT) {Alanine transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP), GGT}, lipid profile, and glycemic status in patients with T2DM.

Materials and Methods:

After taking Necessary permission from the institute ethical committee, Research review Board and Department of Endocrinology/Medicine, the study was conducted at Central Lab, Department of Biochemistry and Jaipur and Diabetes Clinic and Medical OPD, SMS Medical College and hospital, Jaipur. This study was a hospital based comparative Cross sectional study and sampling for the study was done from period from May 2021 to December 2022. An informed written consent was obtained from the cases and controls. 30 Type 2 DM patients aged 40-70 years were taken as cases. Age Matched healthy individuals willing to participate in the study giving written consent were taken as controls.

Patients with the following condition: Pancreatitis, pancreatic trauma, biliary tract disease, intestinal obstruction, salivary gland lesion, renal insufficiency, DKA, Neoplastic disease and TB were excluded. Patients with smoking or alcohol abuse and those taking drugs like hydroclorthiazides, anticonvulsants, birth control pills, statins, acetaminophen etc. were also excluded.

Selection of subject was based on inclusion and exclusion criteria; matched controls and cases were included in the present study after obtaining informed consent. A

proforma was used to record relevant information and patient's data. The blood samples of the patients of type-2 DM and healthy subjects, were taken in EDTA vials (HbA1C) and plain vials (Biochemistry) in morning after overnight fasting. Grossly hemolyzed and lipemic samples were excluded. The plain vial samples were left standing to clot for 30 min; after that, Serum was separated immediately at 3000 rpm centrifugation for 10 min and analyzed on fully automated analyzer Beckman Coulter AU-680. Quantitative data analyzed in the form of mean with standard deviation, as & when required suitable test of significance used to infer data. Levels of statistical significance set at a P value<0.05.

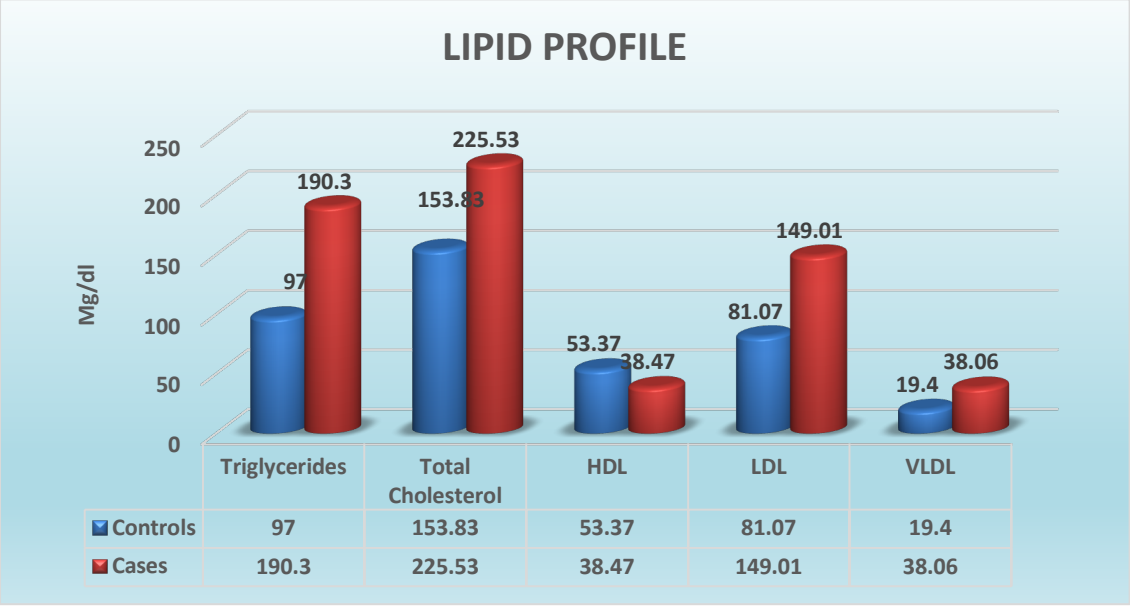
Results

The characteristics of the studied population, including age, the mean levels of blood sugar and HBA1c are shown in Table 1.

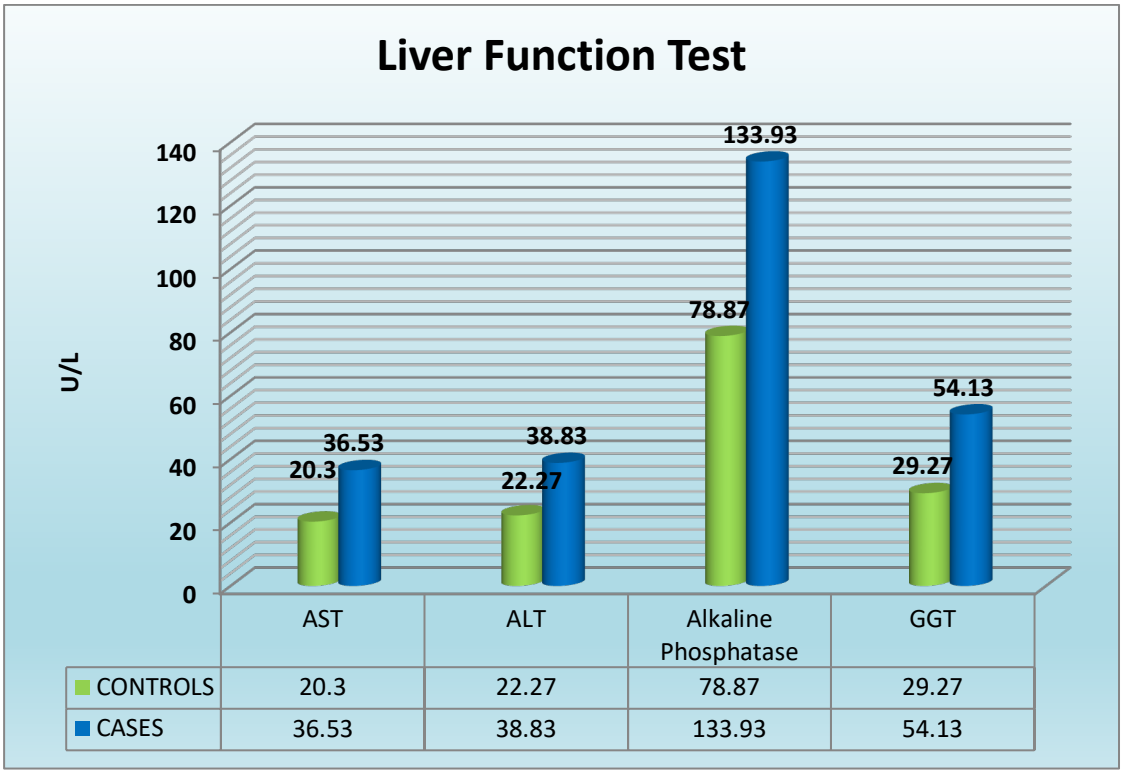
Table 1: Statistical Indices of the study

Test/ Parameters	Cases (n=30)	Controls (n= 30)	P value
Age (years)	53.27 ± 7.39	52.47 ± 8.26	0.347 (NS)
Fasting Blood Glucose (mg/dl)	85.63 ± 13.91	155.20 ± 23.21	< 0.01 (S)
HBA1C (%)	5.18 ± 0.73	7.74 ± 0.72	< 0.01 (S)
Triglycerides (mg/dl)	97.00 ± 29.81	190.30 ± 27.02	< 0.01 (S)
Total Cholesterol (mg/dl)	153.83 ± 26.15	225.53 ± 24.77	< 0.01 (S)
HDL (mg/dl)	53.37 ± 7.07	38.47 ± 5.89	< 0.01 (S)
LDL (mg/dl)	81.07 ± 28.72	149.01 ± 25.25	< 0.01 (S)
VLDL (mg/dl)	19.40 ± 5.96	38.06 ± 5.40	< 0.01 (S)
T. Bilirubin (mg/dl)	0.72 ± 0.26	0.70 ± 0.22	0.3938 (NS)
AST (U/L)	20.30 ± 7.00	36.53 ± 7.59	< 0.01 (S)
ALT (U/L)	22.27 ± 7.95	38.83 ± 10.08	< 0.01 (S)
Alkaline Phosphate (U/L)	78.87 ± 23.01	133.93 ± 31.07	< 0.01 (S)
GGT (U/L)	29.27 ± 7.60	54.13 ± 11.78	< 0.01 (S)

This table shows that mean Lipid Profile levels for cases was higher than that for Controls (Graph 1). The value was statistically significant (p value < 0.01). Similarly the liver enzymes were also higher in cases as compared to controls (Graph 2).



Graph 1: Comparison of Mean Lipid Profile levels between Cases and Controls



Graph 2: Comparison of Mean LFT levels between Cases and Controls

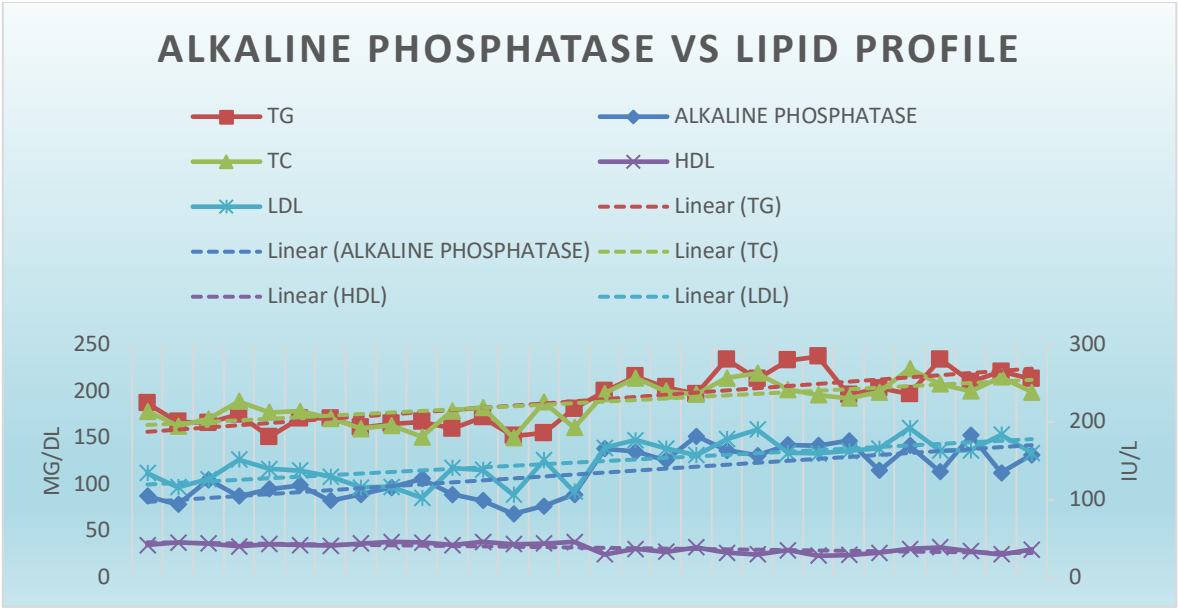
Statistical Correlations between Alkaline Phosphatase and Lipid Profile:

Table 2: Statistical Correlations between Alkaline Phosphatase and Lipid Profile

Parameter	P value	R Score	R^2	Significance
TG	<0.001	0.7741	0.5992	S
TC	<0.001	0.7179	0.5154	S
HDL	<0.001	-0.7691	0.5915	S
LDL	<0.001	0.7183	0.516	S

*Data analysis using Pearson correlation analysis

The above table shows statistically significant Positive correlation between Alkaline Phosphatase and Triglycerides, Total Cholesterol and LDL. However statistically significant Negative correlation is seen between Alkaline phosphatase and HDL. (Graph 3).



Graph 3: Pearson correlation between Alkaline Phosphatase and Lipid Profile

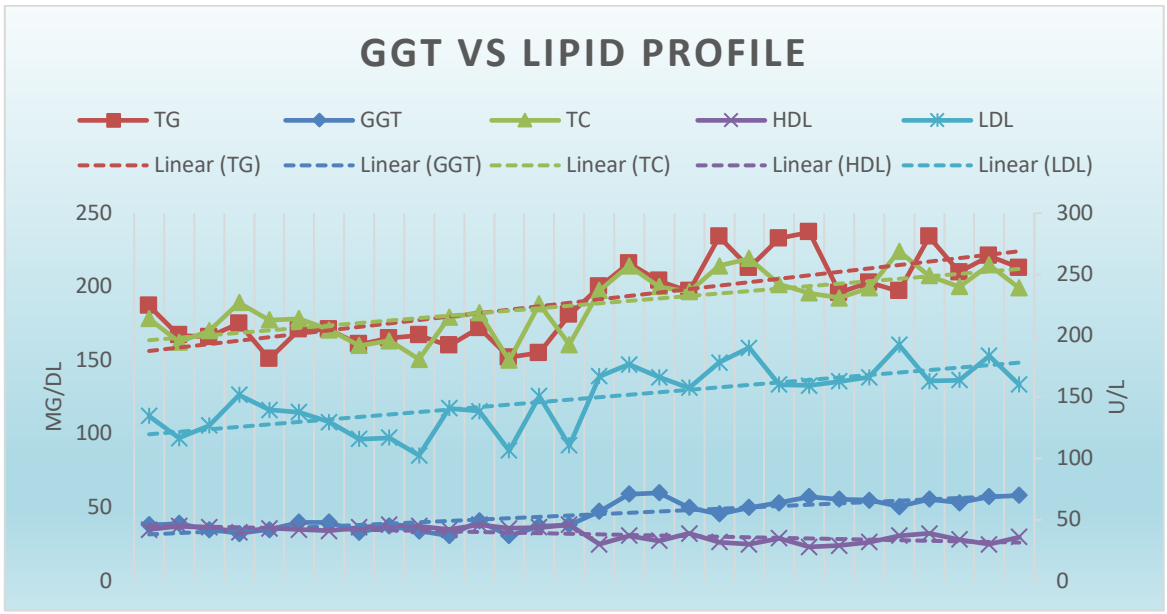
Statistical Correlations between GGT and Lipid Profile:

Table 2: Statistical Correlations between GGT and Lipid Profile

Parameter	P value	R Score	R^2	Significance
TG	<0.001	0.8588	0.7375	S
TC	<0.001	0.7782	0.6056	S
HDL	<0.001	-0.785	0.6162	S
LDL	<0.001	0.7624	0.5813	S

*Data analysis using Pearson correlation analysis

The above table shows statistically significant Positive correlation between GGT and Triglycerides, Total Cholesterol and LDL. However statistically significant Negative correlation is seen between GGT and HDL. (Graph 4)



Graph 4: Pearson correlation between GGT and Lipid Profile

Discussion

The term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long– term damage, dysfunction and failure of various organs. This metabolic disorder (diabetes) affects many organs, including the liver, which plays a key role in the regulation of carbohydrate, lipid, and protein metabolism. The present work was designed to estimate the lipid profile and liver enzymes and to find the association between them in type 2 diabetes patients.

In our study, 30 Type 2 Dm cases were compared with 30 controls. the mean age in control group 53.27 ± 7.39 years was slightly higher than cases group (52.47 ± 8.26 years) (Table 1, Graph 1). This difference was statistically not significant (p value = 0.347). The incidence of diabetes is increasing day by day, and an increase in prevalence rate occurs in developing countries. Studies showed that most of the people aged 45-64 years in developing countries and people of age ≥65 years in developed countries suffer from diabetes.[15]

The mean Triglycerides for controls was 97.00 ± 29.81 mg/dl and for Cases was 190.30 ± 27.02 mg/dl which was statistically significant (p value < 0.01). The mean Total Cholesterol for cases was 225.53 ± 24.77 mg/dl and for Controls was 153.83 ± 26.15 mg/dl. The mean value of TG was higher for Cases when compared to controls. The mean HDL levels for cases 38.47 ± 5.89 mg/dl was lower than that for Controls 53.37 ± 7.07 mg/dl. The mean LDL levels for cases 149.01 ± 25.25 mg/dl was higher than that for Controls 81.07 ± 28.72 mg/dl.

Our findings are mainly in agreement with two landmark studies namely the Framingham Heart Study[16] and the UK Prospective Diabetes Study (UKPDS)[17]. In both studies T2DM subjects compared to those without T2DM, had higher plasma Tg levels and lower HDL-C levels. Moreover, results from the pan-European Survey, USA, China, and India are also in agreement with our findings regarding high Tg and low HDL-C levels in prediabetic subjects.[18-19] Diabetic dyslipidemia includes quantitative as well as qualitative and kinetic lipoprotein derangements, all of which contribute to accelerated atherosclerosis.[20] In type 2 DM, as a consequence of insulin resistance, the free fatty acid (FFA) flux from the adipocytes is increased. This leads to an increased supply of FFA to liver, and therefore increased lipid (VLDL and TGs) synthesis within the hepatocytes. Together with defective hepatic clearance of lipoproteins, this plays a key role in the causation of dyslipidemia seen in type 2 DM (elevated TGs, low HDL-C, and increased small dense oxidized LDL particles). Diabetic dyslipidemia is an established trigger for atherogenesis and macrovascular disease.[21] Diabetic dyslipidemia further worsens in the postprandial state with additive adverse effect of postprandial hyperglycemia.

The mean AST level for cases was 36.53 ± 7.59 U/L and for controls was 20.30 ± 7.00 U/L (p value < 0.01). The mean ALT level for cases was 38.83 ± 10.08 U/L and for controls was 22.27 ± 7.95 U/L (p value <0.01). The mean Alkaline phosphatase level for cases was 133.93 ± 31.07 U/L and for controls was 78.87 ± 23.01 U/L (p value<0.01). The mean GGT level for cases was 54.13 ± 11.78 U/L and for controls was 29.27 ± 7.60 U/L (p value<0.01). The results were statistically significant.

Our findings were in line with a study conducted in India by Sunitha et al in 2015[22] in which the elevation of AST and ALT were statistically associated with T2DM whereas GGT did not show significant correlation. Similar results were in by Belay Z et al[23] in 2014 which

showed that the mean values of, ALT, AST, ALP, total bilirubin, direct bilirubin and serum glucose were significantly higher in T2DM patients as compared with non-diabetic controls (P<0.05). also, Idris AS et al[24] reported that the mean values of ALT, AST and GGT hepatic enzymes were significantly higher in T2DM patients than in controls (P<0.05). In a UK cohort study of 959 diabetic patients, 15.7% had raised ALT, 10.4% had increased ALP and only 3.9% had elevated bilirubin levels.[25] Elevated levels of liver marker enzymes among T2DM cases may be due to increases in glycogen/insulin effect on liver cells. The increase of glycogenolysis (breakdown of stored glycogen) and gluconeogenesis (glucose production from non-carbohydrate precursors) becomes the primary metabolic pathway.[26] An abnormal accumulation of fat and its mobilization in hormone-sensitive tissues (liver) and hepatocytes demonstrate a metabolic switch through insulin resistance identified earlier than the fasting elevation of blood sugar. The overloaded release of free fatty acids due to insulin resistance induces fat mobilization and results in the toxicity of hepatocytes.[22]

We observed significant hyperglycemia, hyperlipidemia with elevated ALT, AST, ALP and GGT in diabetes patients. Our study is consistent with the study of Han Ni, who reported elevated determinants of liver function tests with hyperlipidemia in T2DM.[27] Adeniran et al. investigated that increased ALT and AST with dyslipidemia in patients from Nigeria were diagnosed with T2DM.[28] Liver as a central organ involved in carbohydrate and lipid metabolism and due to insulin resistance in diabetes, its function get disturbed. Insulin contributes proinflammatory effect to liver abrasion. Hyperlipidemic profile is observed due to increased transportation of fat to liver with respect to decreased oxidation. The impairment of normal process of synthesis and elimination of triglycerides may progress to fibrosis, cirrhosis and hepatocellular carcinoma.[29] Reason behind the pathogenesis of NAFLD appears to be insulin resistance which results lipolysis and excess deposition of fat on liver and together create inflammatory affect, oxidative stress and lead to elevate liver enzymes.[30]

Conclusion

To conclude our findings, patients with Type 2 DM was associated with significantly higher total cholesterol, LDL C, VLDL C and triglyceride levels as compare to normal. HDL cholesterol value is significantly lower in hypertensives than normal. This clearly shows that patients with Type 2 DM are at increased risk of cardiovascular events as compare to normal subjects. These patients have significantly altered Liver function tests namely AST, ALT, ALP and GGT when compared with controls. Although the rise was not alarming, but we can conclude that liver may be intimately involved in the pathogenesis of type 2 DM and LFTs may serve as valuable indicators for the risk and progression of future diabetes. Early recognition and appropriate treatment of significant postprandial dyslipidemia and altered LFT's is of paramount importance in diabetics so as to reduce impending complications.

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