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Research Article

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Association between Lipid Profile and Liver Function Tests in Diabetic Patients

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ABSTRACT

It has been observed metabolically as well as by many studies that Diabetes Mellitus, especially Type 2 Diabetic patients have hyperlipoproteinemia. Elevated lipid profile is a common findings in many established diabetic patients. Liver is the sole site for carbohydrates and lipid metabolism. Any dysfunction in liver may lead to altered metabolism of both glucose and lipids. Hence significant relationship must exist between lipid profile and liver function tests. Any derangement in liver function may proportionately affect lipid parameters. All the patients selected for this study were on oral hypoglycemic drugs. The results obtained for the 100 patients studied gave a very good correlation between lipid profile and all the Liver Function Tests as well as to HbA1c, confirming that lipid profile analytes are indeed associated with liver function tests as well as to glycosylated hemoglobin.

Key words: *- Type 2 DM, LFT, HbA1c, Lipid profile.*

INTRODUCTION

Cholesterol is a primary component of plaques found in atherosclerosis and is therefore the major risk factor for the rapid progression of Coronary Artery Disease (CAD). High blood cholesterol may be inherited or may result from such other conditions as biliary obstruction, diabetes mellitus (DM), hypothyroidism, and nephrotic syndrome. Cholesterol is carried in the blood mainly as lipoproteins.

Liver Function Tests (LFTs), are a group of blood tests that detect inflammation and damage to the liver. LFT help determine the health of liver by measuring analytes such as proteins, enzymes, or bilirubin. An abnormal result indicates a problem with the liver, and may help to identify the cause. It helps to diagnose liver disorders and symptomsleading to liver diseases. The pattern of blood results may help to identify the disorder causing the problem. In health care delivery systems worldwide, cases of DM and its associated clinical conditions are increasing on daily basis. It is present in about 4% of the world population and 382 million individuals are with DM as of 2013 end and it may increase to 592 million by the year 2035. The liver helps to maintain normal blood glucose concentration in the system. This liver function is deranged and liver enzymes abnormalitiesare observed in Type 2 Diabetes Mellitus (type 2 DM) and in obese individual. Lipid profile remains one of the corner stone of assessing patients suspected of having risk of developing CADin Type 2 DM and is associated with abnormalities of lipoproteins that, among other factors, might be responsible for the increased incidence of Coronary Heart Diseases (CHD) & CAD. This study is an attempt to find statistically significant association between lipid profile and liver function tests.

LITERATURE REVIEW

Type 2 DM is associated with dyslipdemia, insulin resistance and non alcoholic fatty liver disease (NAFLD). The presence of type 2 DM induced hyperglycemia results in significant increase in lipid profile, oxidative stress markers and inflammatory mediators in patients with NAFLD and normal liver

function tests. Research studies are required to evaluate the benefit of adding suitable antioxidant and anti-inflammatory drugs to the treatment regimen for this group of patients. In addition, regular monitoring of blood glucose levels and liver function tests should be advised to this category of patients to reduce liver fat deposition and to avoid the development of non alcoholicsteatohepatitis (NASH), cirrhosis or liver cancer and their related complications[1].

Elevated Alanine Transaminase (ALT) is not uncommon in Type 1 diabetes and is associated with NAFLD-related risk factors. Patients with Type 1 diabetes and elevated ALT should be investigated as significant abnormalities may be found which are amenable to interventions[2]. Chronic mild elevation of transaminases are frequently found in type 2 DM patients[3]. Type 2 DM has been linked with dyslipideamia and elevation of some liver enzymes and in fact it has been identified as independent risk factor for development of CHD. The risk of CHD in patients with type 2 DM withLow Density Lipoprotein Cholesterol (LDL-C) and Total Cholesterol (TC) were significantly lower in control than the subject group. A weak negative significant correlation exist between High Density Lipoprotein (HDL) / TC and Alkaline Phosphatase (ALP). There are evidences of dyslipidaemia and elevated liver enzymes in type 2 DM patients seen in Osogbo Nigeria[4]. There is a high prevalence of liver function test abnormalities in type 2 DM, and this is particularly so in the morbidly obese subjects. This is comparable with the reported prevalence in the Western world. Lipid abnormalities were more frequent in this group with liver enzyme derangements[5,6].

The prevalence of NAFLD is higher in type 2 DM patients. Obesity, dysglyce-mia, dyslipidemia and elevated liver enzymes are seen more frequently in fatty liver than non-fatty liver type 2 DM patients[7]. Fatty liver was strongly associated with many features of the insulin resistance syndrome, and follow-up revealed a high potential for reversibility and a benign course[8]. There was no significant difference in the lipid levels with respect togender. No association was found between fatty liver grade, sex and Body Mass Index (BMI). An abnormal level of lipid profile amongst patients with fatty liver have been observed. A case -control study may help to find better understanding of lipid levels among NAFLD subjects[9]. Glycosylated hemoglobin, insulin, andHomeostasis Model of Assessment(HOMA) scores for Insulin Resistance (IR) were all positively correlated with selected liver function markers suggesting the integral role of liver function in the development of (IR). Despite previous data linking elevations in free fatty acid to the development of IR,no relationship between the two variables could be found[10]. Correlation coefficient studies also suggest that the possibility of predicting serum levels of transaminases or triglycerides should be further evaluated, as the results support that theultrasonographic evaluation of the liver may be useful for the diagnosis and follow-up of the patient with NAFLD[11].

NAFLD is considered as the hepatic manifestation of IR syndrome[12]. Omega-3 fatty acid treatment may have beneficial effects in regulating hepatic lipid metabolism, adipose tissue function, and inflammation. Recent studies testing the effects of omega-3 fatty acids in NAFLD are showing promise suggesting that these fatty acids may be useful in the treatment of NAFLD. To date, further research is needed in NAFLD to (a) establish the dose of long-chain omega-3 fatty acids as a treatment model, (b) determine the duration of therapy, and (c) test whether there is benefit on the different component features of NAFLD (hepatic fat, inflammation, and fibrosis)[13]. Ultrasonographic evaluation of the liver is useful for the diagnosis and follow-up of patients with NAFLD[14]. Treatment with angiotensin type 1 receptor blockers (ARBs) is known to improve renal dysfunction and glucose metabolism in obese diabetic animal models and humans[15]. The Cholesterol Enriched diet (EC) group increased the glucose, non-HDL, and TC levels in comparison with the Sedentary and exercise (ES) group. Moreover, the EC group increased the Triglycerides (TG) levels versus the EC group ($p < 0.05$). In addition, ALT levels were increased only by diet treatment. These findings indicates that high-intensity resistance exercise contributed to dyslipidemia in hamsters fed a hypercholesterolemic diet, whereas liverfunction enzymes did not differ in regards to the exercise protocol[16].

IR is established as an independent predictor of a range of disorders such as obesity, hypertension, dyslipidemia, type 2 DM and atherosclerotic cardiovascular diseases. There is an association of hyperinsulinemia with hypertriglycerdemia, low level of HDL-C and high level of LDL-C. In NAFLD,

there is an elevation of Alanine transaminase (ALT), raising the possibility that the prospective relationship between ALT and type 2 diabetes may reflect cross-sectional associations with IR or obesity, and a high prevalence of IR in the first degree relatives of type 2 DM. ALT levels in the first degree relatives of type 2 DM had increased levels of IR, the pathogenesis suggesting increase in ALT levels as seen in IR condition, but, ALT was not statistically significant[17].

Using binary logistic regression analysis, it was found that hypertension, LDL-C, microalbuminuria and NAFLD were significantly correlated with CAD. Among type 2 DM, NAFLD clusters with traditional coronary risk factors. It is a surrogate and fairly reliable marker of risk for CAD amongst type 2 DM patients. Ultrasonographically detected NAFLD is a simple, cheap, and safely assessable parameter for coronary risk stratification in type 2 DM[18].

MATERIAL AND METHODS

The study population consisted of 100 non-hospitalised diabetic patients, both males and females in the age group of 27 to 92 years, who underwent routine Master Health Check Up.

As the sole aim of this study was to find out the association between lipid profile and LFT, we made use of laboratory results available for these patients. All the analytes included in this study were measured using state of art fully automaticanlayser and IFCC reference based test kits. HbA1c test was included to link the above association. Inclusion or exclusion criteria were not followed as this study was to find out an association between lipid profile and LFT.

Statistical Analysis

For statistical analysis of data, a software downloaded from the website http://www.vassarstats.net was used to calculate correlation coefficient (r), students't' distribution (t) and probability (p) between each lipid profile test to LFT and HbA1c.

RESULTS

Table I: Statistical Analysis (r, t & p) for all patients (n=100)

Analytes	r	t	p
TCvs TP	0.2625	2.693	<0.01
TCvs ALB	0.3266	3.421	<0.001
TCvs GGTP	0.2045	2.068	<0.005
TG vs BIL	0.2622	2.689	<0.01
TG vs ALB	-0.3576	-3.791	<0.001
TG vs AST	0.4879	5.533	<0.001
TG vs ALP	0.3934	4.236	<0.001
HDL vs BIL	-0.2354	-2.398	<0.01
HDL vs ALB	0.5563	6.627	<0.0001
HDL vs AST,ALT	-0.254	-2.601	<0.01
HDL vs ALP	-0.3795	-4.061	<0.0001
LDL vs BIL	-0.3043	-3.162	<0.001
LDL vs ALB	0.6092	7.605	<0.0001
LDL vs AST,ALT	-0.2374	-2.419	<0.01
LDL vs ALT	-0.2372	-2.417	<0.01
LDL vs HbA1c	-0.1951	-1.969	<0.05
VLDL vs BIL	0.2999	3.287	<0.01
VLDL vs ALB	-0.1875	-1.89	<0.05
VLDL vs ALP	0.1924	1.941	<0.05
VLDL vs GGTP	0.3274	3.43	<0.01
TGvsHbA1c	0.4011	4.335	<0.0001
LDLvsHbA1c	-0.1951	-1.969	<0.05
ALBvsHbA1c	-0.2240	-2.275	<0.05
ASTVsHbA1c	0.2322	2.636	<0.05
ALPvsHbA1c	0.1887	1.902	<0.05

Table II: Statistical Analysis (r, t & p) for Male patients (n=69)

Analyte	r	t	p
TCvs TB	-0.0712	-0.584	<0.0001
TCvs ALB	0.2000	1.671	<0.05
TCvs GGTP	0.2258	1.897	<0.05
TG vs BIL	0.3374	2.953	<0.01
TG vs ALB	-0.2712	-2.306	<0.05
TG vs GGTP	0.2258	1.897	<0.05
HDL vs BIL	-0.2863	-2.447	<0.01
HDL vs ALB	0.4378	3.986	<0.001
HDL vs ALT,ALP	-0.2155	-1.8065	<0.05
LDL vs BIL	-0.3708	-3.268	<0.001
LDL vs ALB	0.5116	4.874	<0.001
LDL vs ALT	-0.1999	-1.67	<0.05
LDL vs ALP	-0.3272	-2.834	<0.01
VLDL vs BIL	0.4596	2.655	<0.01
VLDL vs DB	0.3146	2.713	<0.01
VLDL vs ALP	-0.3272	-2.834	<0.01
VLDL vs GGTP	0.3375	2.935	<0.01
TGvsHbA1C	0.2518	2.13	<0.05
VLDLvs HbA1C	0.2346	1.975	<0.05
TPvsHbA1C	-0.2295	-1.93	<0.05
ASTvs HbA1C	0.0023	0.019	<0.05

Table III: Statistical Analysis (r, t & p) for Female patients (n=31)

Analyte	r	t	p
TCvs ALB	0.5330	3.392	<0.01
TG vs BIL	0.6701	3.6843	<0.0001
TG vs ALB	0.5330	3.392	<0.01
TG vs AST, ALT	0.711	6.017	<0.0001
TG vs ALT	0.5890	3.925	<0.001
HDL vsBIL	-0.5241	-3.317	<0.01
HDL vs ALB	0.7099	5.428	<0.0001
HDL vs AST, ALT	-0.3182	-2.664	<0.01
HDL vs ALP	-0.6126	-4.174	<0.001
HDL vs GGTP	-0.5192	-3.271	<0.01
LDL vs BIL	-0.5834	-3.8815	<0.001
LDL vs ALB	0.7389	5.905	<0.0001
LDL vs ALT	-0.4303	-2.567	<0.01
LDL vs ALP	-0.6978	-5.246	<0.0001
LDL vs GGTP	-0.5275	3.344	<0.01
VLDL vs ALB	-0.3962	-2.324	<0.05
VLDL vs ALP	0.4091	2.414	<0.05
TGvsHbA1C	0.5309	3.374	<0.01
DBvsHbA1C	0.3778	2.197	<0.05
ALBvsHbA1C	-0.3690	-2.138	<0.05
ASTvsHbA1C	0.5374	3.432	<0.01
ALTvsHbA1C	0.3231	1.869	<0.05
ALPvsHbA1C	0.4676	2.849	<0.01
GGTPvsHbA1C	0.5202	3.28	<0.01

The statistical parameters obtained for r, t and p values for all patients, females &males are presented in Tables I, II & III respectively.

Table I presents the 3 statistical parameters for all the 100 patients. Very high significant associations ($p<0.0001$) were found between HDL vs ALB, HDL vs ALP, LDL vs TP, ALB, HbA1c vsTG.

In Table II similar data are presented from the results obtained for all the 69 men very good association was observed ($p<0.001$) TC vs TB, HDL vs ALB, LDL vs TB, LDL vs DB, LDL vs ALB.

As per Table III, presented for female patients, highly significant associations were found for the following TG vs Bilirubin, TG vs AST, HDL vs ALB and good significant at $p < 0.001$ was observed for TG vs ALT, HDL vs TP, HDL vs ALP and LDL vs TB.

Negative correlation were observed for most of the comparison.

DISCUSSION

Many studies have been carriedout to link cardiovascular diseases to liver function in Diabetic as well as in non diabetic patients. Type 2 DM are generally prone to elevation in lipidprofile and since glucose and lipid metabolism are handled by liver, a relationship between lipid profile and LFT must exist. Type 2 DM with and without NAFLD are prone to have increased LFT. Our study gives very good association between lipid profile to almost all LFT and the highest is shown between HDL, LDL & VLDL to all LFT. Further dyslipidemia is also linked to LFT and our study findings is supported by previous observations[1,5,6]. Further HbA1c, the best diagnostic marker for long term diabetic control shows significant association to dyslipedemiaAST, ALT & ALP confirming that HbA1c and lipid profile tests are associated to LFT. Previous studies also confirmed that no significant difference between gender in the observed associations[5]. Lipid dearrangement is a frequent findings in all Type 2 DM and hence there must be laboratory diagnostic link between lipid profile & LFT as observed in this study[7,8,9,10].

CONCLUSION

The outcome of this study confirms that

- All Type 2 DM patients should be screened for lipid profile and liver function tests.
- Once LFT are altered, it is suggested that additional tests like lipid profile are done to assess the cardiac function.

In conclusion, lipid profile are prone to alterations in Type 2 DM and hence frequent checking of lipid profile in Type 2 DM may prevent complications in cardiac function. Further analytes like Insulin Resistance (IR), estimated Glucose Disposal Rate (eGDR) may also be included to diagnostically link the analytes to type2 DM.

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