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Research Article

RATIO OF TRIGLYCERIDES TO HIGH-DENSITY LIPOPROTEIN CHOLESTEROL AND MARKERS OF LIVER INJURY IN DIABETES MELLITUS

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ABSTRACT

Objectives: The present study was done to evaluate and compare the triglyceride to high-density lipoprotein (TG/HDL) ratio in subjects with diabetes mellitus (DM) and diabetic prone subjects (impaired glucose tolerance [IGT]) with normal subjects without diabetes. An attempt was also made to correlate TG/HDL with markers of liver injury such as alanine aminotransferase, aspartate aminotransferase, (AST), and alkaline phosphatase (ALP).

Methods: Lab data of 496 patients attending Pushpagiri medical health checkup were obtained. The subjects were grouped into DM: (fasting plasma glucose >126 mg/dl), IGT: (Fasting plasma glucose: 110-126 mg/dl) and normal: (fasting plasma glucose < 110 mg/dl).

Results: Statistically significant difference were observed in levels of TG, low-density lipoprotein (LDL), TG/HDL ratio, AST, ALP between diabetes, IGT and normal subjects. Statistical significance within the groups was tested using *post-hoc* Analysis. The level of TG and TG/HDL ratio was significantly higher in subjects with DM compared to normal subjects. The mean value of total cholesterol and LDL-C was found to be higher in normal subjects than in DM and IGT. AST, ALP values were found to be significantly higher in subjects with IGT than normal subjects.

Conclusion: From this study, it can be concluded that TG and TG/HDL ratio were high in DM and IGT than subjects with normal plasma glucose. Liver injury marker enzymes were found to be high in IGT and is correlated with TG/HDL ratio in DM.

Keywords: Diabetes mellitus, Impaired glucose tolerance, Hypertriglyceridemia, Triglyceride to high-density lipoprotein ratio, Markers of liver injury.

INTRODUCTION

Defects in insulin action and hyperglycemia could lead to changes in plasma lipoproteins in patients with diabetes. Lipoprotein abnormalities commonly present in Type 2 diabetes, include hypertriglyceridemia, and reduced plasma high-density lipoprotein (HDL) cholesterol. In addition, low-density lipoproteins (LDL) are converted to smaller, more atherogenic, small dense LDL that is often found in pre-diabetics (patients with insulin resistance but normal indexes of plasma glucose) [1,2].

Dyslipidemia associated with diabetes mellitus (DM) result from increased plasma concentrations of very LDL (VLDL), deficient lipoprotein lipase activity; increased cholesteryl ester transfer protein activity; and increased flux of free fatty acids in the liver [3]. A fatty liver is often associated with hypertriglyceridemia in people with insulin resistance. Elevated triglyceride (TG) and depressed HDL levels are the defining components of dyslipidemia in nonalcoholic fatty liver disorder (NAFLD). Most individuals with NAFLD in its uncomplicated form (simple steatosis) are asymptomatic. They may progress to more severe manifestations of the NAFLD disease spectrum, including nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and liver failure [4]. Lipotoxicity, oxidative stress, cytokines, and proinflammatory mediators contribute to the progression from steatosis to nonalcoholic steatotic hepatitis [5]. However, patients with NAFLD and NASH are commonly characterized by elevated circulating concentrations of markers of liver injury, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The ratio of AST to ALT has more clinical utility than assessing individual elevated levels. The ratio increases in progressive liver functional impairments.

Many studies were conducted to evaluate the increase in TG level and a decrease in HDL level in patients with DM, but no systematic studies were carried out to correlate TG/HDL with markers of the liver injury in diabetic patients. Hence, this study was conducted to evaluate and compare the TG, TG/HDL ratio in subjects with DM and diabetic prone subjects (impaired glucose tolerance [IGT]) with normal subjects without diabetes. An attempt was also made to correlate TG/HDL with markers of liver injury (ALT, AST).

METHODS

This study was conducted in Department of Biochemistry, Pushpagiri Institute of Medical Science and Research Center, Tiruvalla, Kerala, India.

Retrospective lab data of 496 subjects attending Pushpagiri Medical Health Checkup were obtained. The subjects were grouped into three according to fasting plasma glucose level-based on International diabetes federation criteria.

Group I: DM: (>126 mg/dl) (n=91)
Group II: IGT: (110-126 mg/dl) (n=59)
Group III: Normal: (<110 mg/dl) (n=346)

The lab data of following parameters were obtained-Total cholesterol(TC),TG,HDL,LDL,AST and ALT.TG/HDL was calculated using this values.

Statistical analysis

Statistical significance among three groups were determined using one-way ANOVA.

Within groups, significance was tested using *post-hoc* analysis, Bonferroni test. 95% confidence interval was taken. Correlation between TG/HDL and AST, ALT were tested by calculating Karl Pearson correlation coefficient. $p<0.05$ was considered to be statistically significant.

RESULTS

Age group of 496 subjects included in this study was (20-75) years. Among this 18% was found to be diabetic, 12% was with IGT, and 70% was normal.

Table 1: Levels of lipid profile, TG/HDL, AST, ALT and ALP in diabetes, IGT and normal subjects

Parameter	Diabetes (n=91)	IGT (n=59)	Normal (n=346)	F	p value
TC (mg/dl)	202.48±48.85	202.10±46.78	210.59±40.129	1.958	0.142
TG (mg/dl)	153.11±69.49	143.68±77.51	127.11±74.18	5.07	0.007
HDL (mg/dl)	46.84±10.92	48.32±10.92	49.80±12.14	2.42	0.09
LDL (mg/dl)	126.71±42.23	129.36±42.66	136.98±35.04	3.271	0.039
TG/HDL	3.48±1.8	3.17±1.95	2.80±2.00	4.617	0.01
AST (IU/L)	30.41±17.11	36.86±26.31	29.43±16.17	4.379	0.013
ALT (IU/L)	41.07±23.70	43.07±29.59	39.31±33.09	0.423	0.655
ALP (IU/L)	192.16±49.53	207.61±108.76	180.25±59.64	4.897	0.008

SD: Standard deviation, results are expressed in mean±SD, TC: Total cholesterol, IGT: Impaired glucose tolerance, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, TG: Triglyceride

Table 2: Pearson correlation analysis of TG/HDL with liver injury markers

Groups	AST	ALT	ALP
DM			
Pearson correlation	0.316**	0.304**	0.098
Significant (two-tailed)	0.002	0.003	0.355
IGT			
Pearson correlation	–0.005	0.154	0.092
Significant (two-tailed)	0.972	0.243	0.486
Normal			
Pearson correlation	0.193**	0.288**	0.135*
Significant (two-tailed)	0	0	0.012

**Correlation is significant at the 0.01 level (two-tailed), *Correlation is significant at the 0.05 level (two-tailed), TC: Total cholesterol, IGT: Impaired glucose tolerance, HDL: High-density lipoprotein, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase

The age of diabetic patients ranged from 36 to 75 years, with a mean age of 55 years. There were 59 (65%) males and 32 (35%) females in this group. Age of subjects with IGT ranged from 27-70 years with a mean age of 50.4 years. There were 30 (51%) males and 29 (49%) females in this group. Age of normal subjects was between 20 and 75 with a mean age of 44.8 years. There were 195 (56%) males and 151 (44%) females in this group.

Levels of TC, TG, HDL, LDL, TG/HDL, AST, ALT, ALP in diabetes, IGT and normal subjects are given in Table 1.

Statistically, significant difference were observed in levels of TG, LDL, TG/HDL ratio, AST, ALP between diabetes, IGT and normal subjects. However, the significant difference was not observed between levels of TC, HDL, and ALT between the three groups.

Statistical significance within the groups was tested using *post-hoc* analysis. The levels of TG and TG/HDL ratio were significantly higher in subjects with DM compared to normal subjects. No such differences were observed between subjects with diabetes and subjects with IGT.

The mean value of TC and LDL was found to be a higher in normal subjects than in DM and IGT. AST, ALP values were found to be significantly higher in subjects IGT than normal subjects.

Correlation of TG/HDL with AST, ALT, and ALP is given in Table 2.

A statistically significant positive correlation was observed for TG/HDL with AST and ALT in subjects with DM. In normal subjects, TG/HDL showed statistically significant positive correlation with AST, ALT, and ALP. No such, correlation was observed in subjects with IGT.

DISCUSSION

DM, the most important independent risk of atherosclerosis, is by far the leading cause of death among patients with Type 2 diabetes. The cluster of lipid abnormalities associated with Type 2 diabetes is defined by a high concentration of TG and small dense LDL and a low concentration of HDL cholesterol. Plasma LDL cholesterol levels are generally normal.

In our study, we observed a statistically significant increase in TG, TG/HDL ratio, in diabetes and IGT group than in normal subjects. In studies conducted by Goldberg and Haffner *et al*., hypertriglyceridemia and reduced plasma HDL cholesterol were observed in Type 2 diabetes and pre-diabetes. There are several reasons for the decrease in HDL found in patients with diabetes. Increased concentrations of plasma VLDL drive the exchange of TG from VLDL for the cholesteryl esters found in HDL. Thus, the etiology of the hypertriglyceridemia and reduced HDL can be accounted for; CETP-mediated exchange of VLDL-TG for HDL cholesteryl esters is accelerated in the presence of hypertriglyceridemia [6].

In the present study, an attempt was also made to evaluate the level of the liver injury marker enzymes in the three groups and to correlate TG/HDL ratio with liver enzymes. We observed that liver injury marker enzymes were significantly high in IGT than normal subjects and showed a positive correlation with TG/HDL ratio in diabetic and normal subjects. These results are supported by previous prospective studies reporting strong associations of elevated liver enzymes (particularly serum GGT levels), as surrogate markers of NAFLD [7,8] with the occurrence of Type 2 diabetic patients. In a study conducted by Vernon *et al*., there is a very high prevalence of NAFLD in individuals with Type 2 DM [9]. Elevated TG and depressed HDL levels are the defining components of dyslipidemia in NAFLD [5].

CONCLUSION

From this study, it can be concluded that TG and TG/HDL ratio, which are independent risk factors for CAD, were high in DM and IGT. Liver injury marker enzymes were found to be high in IGT and is correlated with TG/HDL ratio in DM. This study emphasizes the need for the prevention and control of hypertriglyceridemia in DM and IGT so that the risk of developing CAD and NAFLD will be reduced. Since dyslipidemia is related to lifestyle, reduction in TG levels and better HDL levels can be achieved through lifestyle modifications such as exercise, diet, weight reduction and drugs.

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