TRIGLYCERIDE LEVELS AND ITS CORRELATION WITH CAROTID INTIMA-MEDIA THICKNESS

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ABSTRACT

The aim of the study was to determine the relationship between triglyceride (TG) levels and carotid intima-media thickness (IMT). There are very few Indian studies examining this correlation. The study was conducted on 194 persons from Karnataka. 145 were diabetics (74 females and 71 males), the remaining 49 subjects were age and sex matched controls. All the diabetics had an HbA_{1c} of less than 7%. A fasting triglyceride (FTG) value was obtained. Post-prandial triglycerides (PPTG) were measured after a standard test meal (STM). Intimal thickness of common and internal carotid arteries on both sides was estimated using Doppler Ultrasound. Males and females were analyzed separately, and so were diabetics and non-diabetics. Statistical analysis was done using Prism Software Package. P value <0.05 was considered significant.

The mean FTG values were 127.06 mg/dl and 172mg/dl in diabetic women and men respectively. The mean PPTG levels were 152.5mg/dl and 190.14mg/dl in diabetic women and men respectively. The FTG values had significant correlation with postprandial levels in both diabetic men and women. Correlation between FTG and carotid IMT was found. But no significant correlation was found between PPTG values and carotid IMT in any sub-set of population under study.

Since the study included only well controlled diabetics and since there was significant correlation between fasting and post-prandial triglyceride levels, it may be possible to substitute one for the other. Secondly there was a correlation between fasting triglyceride levels and carotid intima-media thickness. Larger studies are needed to confirm this.

KEY WORDS: Triglyceride levels, Carotid intimamedia thickness, Type 2 diabetes.

INTRODUCTION

Macrovascular disease is a major cause of death in diabetic individuals. It is also known that

dyslipidemia has a direct relation with the development of atherosclerosis. In recent times, the triglyceride (TG) level has emerged as an independent risk factor for atherosclerosis (1, 2). Most studies have examined the triglycerides in the fasting state. However, diabetes is particularly a post-prandial metabolic disorder. and hypertriglyceridemia is a major lipoprotein abnormality (3, 4). Serum TG levels are generally increased for 3-6 hours after a meal. Once postprandial hypertriglyceridemia occurs, it is exacerbated by the next meal and persists for the entire day. Therefore, we are in a post-prandial state for greater periods of the day. We therefore decided to measure both fasting triglycerides (FTG) and postprandial triglycerides (PPTG).

A commonly used atherosclerosis surrogate marker is carotid intima-media thickness (IMT). This is measured by ultrasonography and is a non-invasive and quantitative method for assessing atherosclerosis. There is a direct correlation between carotid IMT and risk for ischemic heart disease (5).

MATERIALS AND METHODS

194 subjects from three centers in Karnataka were included in the study. Ethical committee clearance was obtained and informed consent was taken from all the participants. Out of the 194 persons, 145 were diabetics (74 females and 71 males) and 49 persons served as age- and sex-matched controls. Only those diabetics who had glycosylated hemoglobin (HbA_{1c}) of less than 7% were included to avoid confounding results of triglyceride because of hyperglycemia. The exclusion criteria were uncontrolled diabetes, patients receiving lipid lowering agents and hormone replacement therapy, known cases of hypothyroidism not on thyroxine replacement therapy, patients with chronic complications of diabetes such as nephropathy, hepatic disease, current history of alcoholism, immediately after exercise and existing ischemic heart disease as determined by history and ECG.

The hematological investigations included HbA_{1c}, done by photometric method using Nycocard reader

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11, fasting plasma glucose (after a minimum of 10 hours of fasting) (GOD-POD method), fasting lipid profile, PPTG following 2 hours of a standard test meal and post-prandial plasma glucose. Triglycerides were

tested using a semi-autoanalyser RA 50 by enzymatic spectrophotometry GPO/P method. Assessment of carotid IMT by Doppler studies was done for all the subjects. The standard test meal consisted of 440 Kcals, (60% - carbohydrates, and 20% - fats and proteins each)

Males and females were analyzed separately, and so were diabetics and non-diabetics. Statistical analysis was done using Prism software package. p value < 0.05 was considered significant.

Table 1: Mean Values of Fasting and Post-
Prandial Triglycerides

	Mean FTG	Mean PPTG
DM (Females)	127.06	152.5
DM (Males)	172	190.14

RESULTS

In diabetic women the mean FTG value was 127.06 mg/dl (SD±69.93, range 74-444)(table1, fig1). The mean PPTG level was 152.5 mg/dl (SD±45.76, range 97-234) (table1, fig 3). In diabetic men, the mean FTG value was 172mg/dl (SD±119.09, range 46-647) (table 1, Fig 2). The mean PPTG level was 190.14 mg/dl (SD±86.23, range 77-475(table 1 fig 4). The fasting TG values had significant correlation with postprandial levels in diabetic men (fig 6) (Pearson r = 0.8880, p<0.0001, R squared = 0.7885) and women (fig 5) (Pearson r = 0.8317, p<0.0001, R squared = 0.6917). Correlation between FTG values and carotid IMT was found (Pearson r = 0.9043, p < 0.0001, R squared = 0.8177) (table 2). There was no such correlation in diabetic women. In the postprandial state, there was no significant correlation between triglyceride values and carotid IMT in any subset of the population under study.

Table 2: Correlation of TG with IMT

	Ν	P value
FTG (diabetics)	145	< 0.0001
FTG (controls)	49	NS
PPTG(diabetics)	145	NS
PPTG(controls)	49	NS

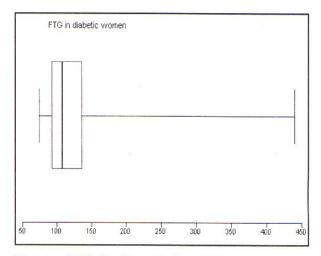


Fig. 1 : FTG (fasting triglycerides) in diabetic women

"x" axis – Triglyceride values in mg/dl "y" axis – Number of diabetic women

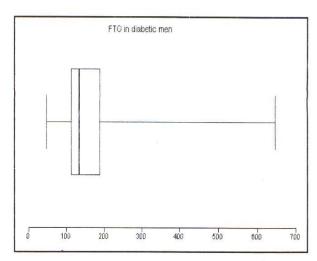


Fig. 2 : FTG (fasting triglycerides) in diabetic men "x" axis – Triglyceride values in mg/dl "y" axis – Number of diabetic men

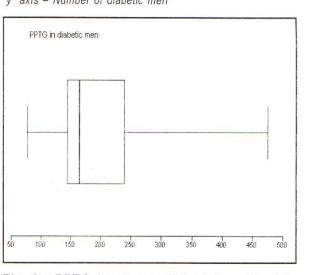


Fig. 3 : PPTG (post-prandial triglycerides) in diabetic women

"x" axis – Triglyceride values in mg/dl

"y" axis - Number of diabetic women

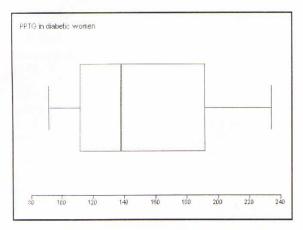


Fig. 4: PPTG (post-prandial triglycerides) in diabetic men

"x" axis – Triglyceride values in mg/dl "y" axis – Number of diabetic men

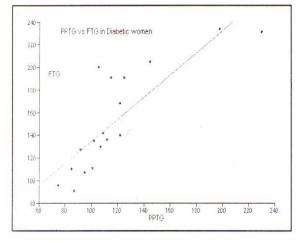


Fig. 5: Correlation of FTG (fasting triglycerides) with PPTG (post-prandial triglycerides) in diabetic women.

"x" axis – PPTG (post-prandial triglycerides) in mg/dl; "y" axis – FTG (fasting triglycerides) in mg/dl

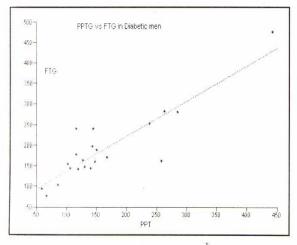


Fig. 6 : Correlation of FTG (fasting triglycerides) with PPTG (post-prandial triglycerides) in diabetic men.

"x" axis – PPTG (post-prandial triglycerides) in mg/dl; "y" axis – FTG (fasting triglycerides) in mg/dl

DISCUSSION

Patients with diabetes have an increased risk of developing cardiovascular disease. The reasons for this are manifold. Hyperglycemia is of course all important. But recently there has been a lot of focus on lipids in general and triglycerides in particular. As mentioned earlier, triglyceride levels are now being accepted as independent risk factors for the development of atherosclerosis. In clinical studies as well as in routine practice, plasma lipids are usually measured in the fasting state and treatment strategies for prevention of cardiovascular disease are based on such measurements. But a large part of our lives are spent between the consumption of regular meals. There are changes in both the composition and concentration of atherogenic lipoproteins in the postprandial state. These postprandial increases in atherogenic plasma lipoprotein concentrations are accentuated in insulin-resistant states. Perhaps the PPTG levels affect atherosclerosis more (6). An internet search seeking to find studies correlating hypertriglyceridemia, type 2 diabetes and carotid IMT yielded just 2-3 studies done in the last few years. Therefore, in this study, we endeavored to find a correlation between fasting and post-prandial triglycerides. We also then studied the correlation of the triglyceride levels with carotid IMT.

Since hyperglycemia itself can raise the triglyceride levels to a significant extent, our study population included only well controlled diabetics who had a glycosylated hemoglobin value of less than 7%. There was a significant correlation between fasting and post-prandial triglyceride levels. This correlation would suggest that one could be substituted for the other.

It is known that early atherosclerotic changes in the vessels can be evaluated by measurement of carotid IMT (7). In fact, a recent study evaluated the relationship between post-prandial hypertriglyceridemia and hyperglycemia and endothelial dysfunction (8). In a study published in 1994, type 2 diabetic subjects had larger carotid IMT and higher levels of triglycerides compared with control subjects (9). In the present study, there was a correlation between FTG and carotid IMT. This has been corroborated in other studies too (2, 10, 11). These same studies also found a correlation between PPTG and carotid IMT. However, a clear cut association between post-prandial triglycerides and carotid IMT was not found in the present study, either in the study population or in the control group. One of the studies done recently on a Chinese type 2 diabetic population also found a significant correlation between raised PPTG and carotid IMT (12). However, in this study a mixed meal test was used and a 4-hour PPTG was performed. In our study, we used a Standard test meal with the major portion coming from carbohydrates. There is no consensus yet of how a standardized postprandial state should be elicited (dose or contents of an experimental meal). We used a 2-hour PPTG on the basis of a pilot study that we performed on 20 patients that showed a good correlation between the 2-hour

PPTG and 4-hour PPTG. Perhaps, the lack of correlation between PPTG and carotid IMT in our study could be explained on the basis of ethnic differences. Larger studies would be needed to confirm this.

In conclusion, it could be said that measurement of fasting triglycerides could be substituted for postprandial

triglycerides, as they correlate well with each other. Fasting triglycerides correlate significantly with carotid intima-media thickness. This serves as an inexpensive and non-invasive marker of early atherosclerosis, which is ultimately a major cause of mortality and morbidity in type 2 diabetics. Triglycerides are an independent risk factor for endothelial abnormality. Larger studies are needed to confirm this, especially in the diabetic population

REFERENCES

- 1. Miller M, Seidler A, Moalemi A, Pearson TA. Normal triglyceride levels and coronary artery disease events. J Am Coll Cardiol 1998; 31; 1252-7
- Koskinen P, Manttari M, Manninen V, Huttenen JK, Heinonen OP, Frick MH. Coronary Heart disease incidence in NIDDM patients in the Helsinki Heart Study. Diabetes Care 1992; 15; 820-5
- Sniderman AD, Scantlebury T, Cianflone K. Hypertriglyceridemic hyper-apo B : The unappreciated atherogenic dyslipoproteinemia in Type 2 diabetes mellitus. Ann Intern Med 2001; 135: 447-59

- Tomkin GH, Owens D. ApoB lipoproteins, diabetes and atherosclerosis. Diabetes Metab Res Rev 2001: 17: 27-43
- O'Leary DH, Polak JE, Kronmal RA, Mnaolio TA, Burke GL, Wolfson SK Jr. Carotid artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults: Cardiovascular Health Study Collaborative Research Group, N Engl J Med 1999: 340: 14-22
- 6. Patsch JR, Miesenbock G, Hopferwieser T, et al. Relation of triglyceride matabolism and coronary artery disease: studies in the post-prandial state. Arterioscler Thromb 1992 : 12 :1336-45
- Handa N, Matsumoto M, Maeda H, et al. Ultrasonic evaluation of early carotid atherosclerosis. Stroke 1990: 21: 1567-72
- 8. Antonio C, Claudio T, Laura T, et al. Evidence for an independent and cumulative effect of postprandial hypertriglyceridemia and hyperglycemia on endothelial dysfunction and oxidative stress generation. Circulation 2002 : 106;1211-8
- 9. Pujia A, Gnasso A, Irace C, Colonna A, Mattioli PL. Common Carotid arterial wall thickness in NIDDM subjects. Diabetes Care 1994 : 17 (11)
- Shinichi T, Yuko U, Hirotaka N, et al. Association of Postprandial Hypertriglyceridemia and Carotid Intima-Media Thickness in patients with Type 2 diabetes. Diabetes Care 2000: 23: 1401-6
- 11. Kofoed SC, Gronholdt ML, Bismuth J, Wilhjelm JE, Sillesen H, Nordestgaard BG. Echolucent, rupture prone carotid plaques associated with elevated triglyceride rich lipoproteins, particularly in women. Journal of Vascular Surgery 2002 : 36(4) :783-92
- Tian, Hao, Chen, Xiang, Liu, Rei. Association between fasting triglycerides, postprandial triglycerides and Apolipoprotein CIII Gene Polymorphism and Carotid Intima- Media thickness in Chinese Type 2 diabetes. Abstract Book 2003; 63rd Scientific Sessions, New Orleans, USA