A Study to Show Postprandial Hyper Triglyceridemia as A Risk Factor for Macrovascular Complications in Type 2 DM

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ABSTRACT

Introduction: Triglyceridemia is an independent risk factor for coronary artery disease irrespective of total cholesterol and LDL cholesterol or low HDL cholesterol. Various publications have challenged this practice citing postprandial hyper-triglyceridemia as a risk for cardiovascular events.

Material and methods: Two hundred patients with Type 2 diabetes for more than one year between the age group of 30-65 years in this study and 50 healthy subjects without any coincidental illness were selected as controls. Each patient underwent detailed clinical history, physical examination and investigations. Blood samples were taken after 2 hours to measure the postprandial blood glucose levels and triglyceride levels; a third blood sample was collected 4 hours after the meal to measure postprandial triglycerides.

Results: Among the total 200 patients 66 were males (66%) and 34 were females (34%). In the group 1 of the 100 patients were males (68%) and 32 were females (32%).In the group 2 of the 100 patients 64 were males (64%) and 36 were females (36%).In the group 3 of the 50 patients 34 were males (68%) and 16 were females (32%). It was found that there was not much in fasting triglyceridemia; while there was significant difference in patients with evidence of coronary heart disease.

Conclusion: Our results showed that TG levels peaked 4 h after the standardized high-fat meal, corroborating previous studies.

Keywords: Coronary artery disease, Post-prandial triglycerides, Type 2 Diabetes Mellitus

INTRODUCTION

Triglyceridemia is an independent risk factor for coronary artery disease irrespective of total cholesterol and LDL cholesterol or low HDL cholesterol.[1] ATP III guidelines[2] suggest at least 9 hour fasting before estimating lipid profile. Many studies did not agree with this practice. Although this association is not entirely certain, it does raise into question the requirement for obtaining fasting lipoprotein measurements.[2,3]

Raised Triglyceride levels are associated with macrovascular complications has not been investigated in diabetic patients. Further studies have shown postprandial hyper-triglyceridemia as a risk factor for developing cardiovascular events and thus posing a question of whether it is really necessary to obtain fasting lipids.[4-9] Nordestgaard et al[10] established the direct correlation of non-fasting TG and the risk of myocardial infarction, ischemic heart disease, and death in 7,587 women and 6,394 men. The most interesting part is that non-fasting triglycerides levels may be even better predictor of cardiovascular risk as compared to fasting triglycerides[4,10] According to Patsch et al[11] (1992), the postprandial but not fasting TG levels exhibited an association with CAD that was statistically independent and stronger than that of HDL-cholesterol.[11]

Atherosclerosis is a multifactorial disease where atherosclerosis and dyslipidemia are the prominent causes involved.[10-13] It has been proposed that postprandial lipoproteins may be better indicators of deranged lipoprotein metabolism and hence of atherosclerosis and CHD.[14-17] When the fat content in a test meal increased from 25 to 45%, pTG levels only increased by 10%.[10,11] This result implies that a special test meal is not necessary for the evaluation of postprandial hypertriglyceridemia. Because we wanted to investigate whether pTG levels were associated with atherosclerosis in normal daily life, we gave our subjects a test meal that resembled their daily diets.

We aimed to investigate the role of postprandial hyper-triglyceridemia in type 2 diabetic patients with and without macro vascular disease and establish their role as a risk factor for macro vascular complications.

MATERIAL AND METHODS

This case control study was done at SVS Medical College and hospital, Mahabubnagar in Telangana State between 1-8-2012 and 31-7-2014. Two hundred patients with Type 2 diabetes for more than one year between the age group of 30-65 years in this study and 50 healthy subjects without any coincidental illness were selected as controls. The cases were sub divided into two groups based on the history of macro-vascular complications. Group I comprises of patients with type 2 diabetes mellitus with history of macro-vascular complications such as ischemic heart disease and or cerebrovascular disease, Group II comprises of patients with type 2 diabetes mellitus, of more than 1-year duration without evidence of ischemic heart disease, cerebrovascular disease and peripheral vascular disease, Group III comprises of normal healthy age and gender matched

Complication	Group-1: Diabetes with complication	
	Number	%
MI	28	28
CVA	32	32
Both	40	40
Total	100	100

Table-1: Distribution of subjects based on complication in group 1

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Parameter	Grp-1: Diabetes with complication		Grp 2: Diabetes without complication		Grp 3: Controls	
	MEAN (mg/dL)	SD	MEAN (mg/dL)	SD	MEAN (mg/dL)	SD
FBS	205.2	71.4	150.6	26.6	85.1	9.07
PPBS	294.68	103.48	204.16	45.62	114.44	13.8
Urea	29.64	5.2	27.92	3.55	26.8	2.91
Creatinine	1.07	0.19	0.89	0.14	0.84	0.16
Total Cholesterol	196.6	32.9	176.2	30.17	156.8	19.08
Triglyceride Fasting	223.43	61.8	199.6	56.9	126.08	24.86
HDL	31.8	7.5	31.6	6.69	44.92	5.23
LDL	120	30.2	103.29	28.3	86.6	21.7
VLDL	44.6	12.3	39.9	11.3	25.2	4.97
Triglyceride Post Fat Meal	407.2	109.8	337.6	80.7	211.3	40.8

Table-2: Mean ± SD values of studied parameters in Diabetes with complication, diabetes without complication and controls.

Parameter	Grp-1 vs Grp 2 vs		Grp 2 vs
	GRP 2	GRP 3	GRP 3
FBS	<0.001	<0.001	<0.001
PPBS	<0.001	<0.001	<0.001
Urea	0.322	0.049	0.616
Creatinine	0.002	<0.001	0.605
Total Cholesterol	0.042	<0.001	0.057
Triglyceride Fasting	0.257	<0.001	<0.001
HDL	0.994	<0.001	<0.001
LDL	0.097	<0.001	0.102
VLDL	0.259	<0.001	<0.001
Triglyceride Post Fat Meal	0.014	<0.001	<0.001

Table-3: ANOVA multiple comparison of significance

patients without any history of diabetes, or any evidence of risk factors. Blood drawn from the cases on fasting, 2 and 4 hours after normal food. Serum was used to measure total cholesterol, triglycerides, HDL Cholesterol, LDL cholesterol, serum Urea, Serum Creatinine, fasting blood glucose levels. The patients were given regular normal diet. Blood samples were taken after 2 hours to measure the postprandial blood glucose levels and triglyceride levels; a third blood sample was collected 4 hours after the meal to measure postprandial triglycerides. All these cases subjected to clinical examination and routine investigations. The subjects below 30 years and above 65 and new diabetic cases were excluded from this study.

STATISTICAL ANALYSIS

Data obtained was analyzed by SPSS statistical software (v 17.0) ANOVA was used to compare the 3 groups and significance was estimated using the F value in between different groups. Other statistical tests such as x 2-test (Chi square test) were applied for nominal data. The level of significance was estimated by applying the, probability value (p). $p < 0.05$ was taken as significant and < 0.01 was taken as highly significant.

RESULTS

The patients had a minimum age of 30 years to a maximum of 63 years. The mean age of the patients in the three groups were not significantly different from each other ($F = 0.25$, $p > 0.05$). Chi square value was 0.12 with a 'p' value greater than 0.05 was noticed amongst the three groups. The mean BMI was significantly more in group 1 compared to group 3 ($p = 0.039$) there was no significant difference in the mean BMI between group 3 and group 2 ($p = 0.118$), group 2 and group1 ($p = 0.878$).

In group 1, 28 patients (28%) had suffered with MI as the complication, 32 patients (32%) had suffered with cerebrovascular accident (CVA) as the complication and 40 patients (40%) had suffered with both MI and CVA as the complication.

The mean values for FBS, PPBS, and total cholesterol, Creatinine and post meal triglycerides are significant higher in diabetes with complication group compared to diabetes without complication and controls. The mean values of fasting triglycerides, LDL, VLDL was not significantly higher in diabetes with complication group compared to diabetes without complication.

In order to assess the maximum sensitivity, specificity, and diagnostic efficiency of triglycerides in identifying abnormality the best cut off values are calculated using ROC analysis. Best cut off values are established by selecting a point closer to top left hand curve that provides greatest sum of sensitivity and specificity as shown in table-4. Diagnostic efficiency is defined as the portion of all currently classified as having or not having complications.

$$\text{Diagnostic efficiency} = \frac{\text{True Positive} + \text{True Negative}}{\text{Total No. Of Patients Evaluated}}$$

Best cut off values for different parameters along with sensitivity, specificity and diagnostic efficiency values for group 1 and group 2 are presented in table-4.

At 167.5 mg/dl fasting triglycerides levels were able to differentiate presence of complications in diabetes with 88 % sensitivity and 40 % specificity compared to post prandial triglycerides which had 80% sensitivity and 60 % specificity and an overall diagnostic efficiency of 70 % at 325 mg/dl.

DISCUSSION

Usually TG levels were estimated I fasting state, but many a study proved post prandial TG was more harmful. This testing of post prandial TG levels was cumbersome and not practical routinely in routine practice. Obesity by itself is considered a predictor of adverse lipid metabolism alterations on fasting state; however, few studies correlated the obesity with postprandial TG lipid profile. Our results showed that TG levels peaked 4 h after the standardized high-fat meal, corroborating previous studies [18 and 4] (Boquist et al.[18] 1999, Bansal et al.[4] 2007). Stampfer and colleagues[19] (1996) showed that plasma TG levels measured 3 to 4 h after a meal were better than fasting plasma TG levels at predicting future cases of myocardial infarction.

Some studies showed post prandial increase in normal

Parameter	Best cut off values	Sensitivity	Specificity	Diagnostic efficiency
Duration of diabetes	7.2yrs	80 %	84 %	82%
Triglycerides fasting	167.5 mg/dl	88%	40%	64 %
Triglycerides post fat meal	328.5 mg/dl	90 %	86 %	86%

Table-4: Best cut off values, diagnostic efficiency, sensitivity, specificity, in discriminating diabetes with complication and diabetes without complication.

Study	Group I	SD	Group II	SD	Group III	SD
Teno et al[24] (2000)	3.04 mmol/ L	1.24	1.41 mmol/ L	0.24	1.25 mmol/ L	0.45
Madhu et al[25] 2005	187.1 mg/dL	63.45			156.85 mg/dL	76.57
Nordestgaard et al[10] 2007	177.0 mg/dL, males		265.5 mg/dL, females			
V Kumar et al[26] 2008	145.0 mg/dL	85.3	93.3 mg/dL	25.8	95.8 mg/dL	22.4
Rathore et al[27] 2014	2.24 mmol/ L	0.51			1.28 mmol/ L	0.16
Kavitha et al[28] 2015	200 mg/dL					
Present study	223.43	61.8	199.6 mg/dL	56.9	126.08 mg/dL	24.86

Table-5: Earlier studies compared with the present study of Fasting triglyceride levels

Study	Group I mg/dL	SD	Group II mg/dL	SD	Group III mg/dL	SD
Teno et al[24] 2000	4.41 mmol/L	2.67	2.96 mmol/L	0.48	1.30 mmol/L	0.50
Madhu et al[25] (2005)	549.68 mg/dL	38.24			294.75 mg/dL	17.6
Nordestgaard et al[10] (2007)	264.6 males		353.1 females			
V Kumar et al[26] (2008)	346.5 mg/dL	48.04	206.0 mg/dL	66.4	121.4 mg/dL	25.4
Rathore et al[27] 2014	3.21±0.76				2.28±0.17	
Kavitha et al[28] 2015	250					
Present study	407.2 mg/dL	10.8	337.6 mg/dL	80.7	211.3 mg/dL	40.8

Table-6: Earlier studies compared with the present study of Post lipid meal triglyceride levels

individuals. In 2003, So[20] and colleagues have characterized patterns of lipid profile changes postprandially in healthy Filipino volunteers after oral fat challenge test. This study showed that triglyceride levels have increased to peak levels up to 274 to 310 mg/ dL at 4 to 5 hours after a high fat meal. At the same the same study showed serum LDL levels decreased after meals.[20] Ginseberge[21] et al thought that a delay in clearance of TG- rich particle may cause the TG elevation after meal. Bravo[22] and others had stated a reference interval values for nonfasting TG as follow (in mmol/L): healthy < 2.0 (2 × 88.5); intermediate 2.1 to 2.7; altered > 2.8; but this observation was not on patient with any cardiovascular disease. All the postprandial TG values up to the 12th hour of observation was significantly higher than the baseline at a range of 23.86 to 72.02 mg/dL (0.27 to 0.82 mmol/L). Boccalondro et al,[23] had shown post prandial elevation was more relevant in ischemic heart diseases as compared to healthy cases. Tables 5 and 6 show the comparison of the present study with earlier available studies.

CONCLUSION

It has been noticed in our study the importance of post prandial TG levels and this finding was consistent with many earlier studies. There has been a lot of studies in support of this finding. We recommend a pp TG estimation in evaluation CAD especially in diabetic cases. a paradigm shift in the diagnosis and management of dyslipidemia seems to be inevitable. A random lipid level determination at clinic, especially 4 hours after normal meals is an ideal way to know the risk of CAD in T2 DM cases. We recommend that in future studies, a larger population size be recruited to represent the general population and in cases with already established CAD.s. A series of studies on high risk patients that would document recurrence of CV events despite their compliance to the standard dyslipidemia treatment and normal fasting lipid profile, will further strengthen the importance of postprandial lipemia.

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REFERENCES

1. Hokanson JE and Austin MA. Plasma triglyceride level is a risk factor for cardio-vascular disease independent of high density lipoprotein cholesterol levels: a Meta analysis of population based prospective studies. J Cardiovasc. Risk. 1996;3:213–219.
2. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): JAMA. 2001;285:2486.
3. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report: Circulation. 2002;106: 3143-421.
4. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM and Ridker PM: Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. JAMA. 2007;298:309-16.
5. Eberly LE, Stamler J and Neaton JD. Relation of triglyceride levels, fasting and nonfasting, to fatal and nonfatal coronary heart disease. Arch Intern Med. 2003; 163:1077-83.

6. Langsted A, Freiberg JJ and Nordestgaard BG. Fasting and nonfasting lipid levels: influence of normal food intake on lipids, lipoproteins, apolipoproteins, and cardiovascular risk prediction. Circulation. 2008;118:2047-56.
7. Mora S, Rifai N, Buring JE and Ridker PM. Fasting compared with nonfasting lipids and apolipoproteins for predicting incident cardiovascular events. Circulation. 2008;118:993-1001.
8. Sidhu D and Naugler C. Fasting Time and Lipid Levels in a Community-Based Population: A Cross-sectional Study. Arch Intern Med. 2012;1-4.
9. Talmud PJ: Nonfasting Apolipoprotein B and Triglyceride Levels as a Useful Predictor of Coronary Heart Disease Risk in Middle-Aged UK Men. Arteriosclerosis, Thrombosis, and Vascular Biology. 2002;22:1918-1923.
10. Nordestgaard BG, Benn M, Schnohr P and Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease and death in men and women. JAMA. 2007;298:299–308.
11. Patsch JR, Miesenbock G, Hopferwieser T, Muhlberger V, Knapp E, Dunn JK, Gotto Jr AM and Patsch W(): Relation of triglyceride metabolism and coronary artery disease. Studies in the postprandial state. Arterioscler Thromb Vasc Biol. 1992;12:1336-1345.32.
12. Cohen JC, Noakes TD, Benade AJ: Serum triglyceride responses to fatty meals: effects of meal fat content. Am J Clin Nutr 1988;47:825–827.
13. Rosenson RS. Hypertriglyceridemia and coronary heart disease risk: Cardiol Rev 1999;7:342-8.
14. Zilversmit DB. Atherogenesis: A postprandial phenomenon: Circulation. 1979;60:473-85.
15. Bae JH, Schwemmer M, Lee IK, et al.: Postprandial hypertriglyceridemia induced endothelial dysfunction in healthy subjects is independent of lipid oxidation. Int J Cardiol. 2003;87:259-67.
16. Ernst JS, Marie CA, Judith R, et al. Comparison of fasting and postprandial plasma lipoproteins in subjects with and without coronary heart disease. Am J Cardiol. 2001;88:1129–33.
17. Viviane Nogaroto, Marcos R.S. Rodrigues, Marcelo R. Vicari, Mara C. De Almeida, Fábio Q. Milléo, Fábio A. Dos Santos and Roberto F. Artoni High Postprandial Triglycerides Serum Levels: Is Obesity a Good Predictor? Anais da Academia Brasileira de Ciências (Annals of the Brazilian Academy of Sciences). 2015;87:437-445.
18. Boquist S, Ruotolo G, Tang R, et al. Alimentary lipemia, postprandial triglyceride-rich lipoproteins, and common carotid intima-media thickness in healthy, middle-aged men. Circulation. 1999;100:723-728.
19. Stampfer MJ, Krauss RM, Ma J, Blanche PJ, Holl LG and Sacks FM. A prospective study of triglyceride level, low-density lipoprotein particle diameter, and risk of myocardial infarction: JAMA. 1996;s276:882-888.
20. So T, Mercado-Asis L and Zacarias M. A Comparison Of Dose Response Postprandial Lipid Profile Of Healthy Filipino Subjects After An Oral Fat Challenge Test Of Varying Fat Contents. Phill J Internal Medicine. 2004;42: 1-7.
21. Ginsberg HN. New perspectives on atherogenesis: role of abnormal triglyceride-rich lipoprotein metabolism. Circulation. 2002;106:2137-42.
22. Bravo E, Napolitano M, Botham KM. Postprandial lipid metabolism: the missing link between life-style habits and the increasing incidence of metabolic diseases in western countries? Open Trans Med J. 2010;2:1-13.
23. Boccalandro F, Farias J, Boccalandro C and Vaisman D. Frequency of postprandial lipemia after a first acute coronary event (unstable angina pectoris or non-ST-segment elevation acute myocardial infarction) and the effects of atenolol on the lipemia. Am J Cardiol. 2002;90:153-6.
24. Teno S, Uto Y, Nagashima H, Endoh Y, Iwamoto Y, Omori Y and Takizawa T. Association of Postprandial Hypertriglyceridemia with Carotid Intima Thickness in Type 2 Diabetes Diabetes Care. 2000;23:1401–1406.
25. Madhu SV, Mittal V, Ram BK and Srivastava DK. Postprandial lipid abnormalities in type 2 diabetes mellitus. J Assoc Physicians India. 2005;53:1043-6.
26. Vijay Shankar, Harnam Kaur, Kiran Dahiya, MS Gupta. Comparison of Fasting and Postprandial Lipid Profile in Patients of Coronary Heart Disease; Bombay Hospital Journal. 2008;50:445-49.
27. Rathore S, Sarkar P, Varma M and Bidwai. A Clearance of postprandial lipids is delayed in subjects with cardiovascular disease; International Journal of Pharmaceutical, Biological and Chemical Sciences (IJPBCS). 2014;3:35-45.
28. G. Kavitha, S. Sethupathy and P Gunasekharan. To Correlate Postprandial Triglyceride Levels and CIMT after a Fatty meal in Type 2 Diabetes Mellitus patients with and without microalbuminuria International J Sciences and Applied Res. 2015;2:44–46.

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