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Original Article

A Study to Show Postprandial Hypertriglyceridemia as a Risk Factor for Macrovascular Complications in Type 2 Diabetis Mellitus

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Abstract

Introduction: Diabetes mellitus (DM) comprises a group of metabolic disorders that share the phenotype of hyperglycemia with a predisposition to macro- and micro-vascular complications.

Aims: Estimation of fasting triglycerides (TG) levels in patients with Type 2 DM with and without macrovascular complications. Compare postprandial triglyceridemia with already established independent markers such as fasting TG and high-density lipoprotein cholesterol.

Materials and Methods: This case–control study was done at SVS Medical College and Hospital, Mahabubnagar, between 2012 and 2014. In the present study, 75 patients between the age group of 30–65 years were selected, 50 patients with known diabetes were grouped as cases, and 25 healthy subjects without any coincidental illness were selected as control.

Results: The present study was undertaken in the Department of General Medicine, S.V.S Medical College and Hospital, Mahabubnagar.

Conclusion: Macrovascular complications are more commonly observed in type 2 diabetis Mellitus. Chief observation in the present study was that elevated fasting triglyceride level was significantly associated in patients with diabetes.

Key words: Hypertriglyceridemia, Macrovascular complications, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) comprises a group of metabolic disorders that share the phenotype of hyperglycemia with a predisposition to macro- and micro-vascular complications. India is referred to as the world diabetic capital; incidence of DM is rising in alarming proportions. The worldwide prevalence of diabetes has risen dramatically over the past two decades, from an estimated 30 million cases, in 1985, to 177 million, in 2000. Based on current trends, >360 million individuals worldwide will have diabetes by the year 2030. Although the prevalence of both Type 1 and Type 2 diabetes is increasing worldwide, the prevalence of Type 2 diabetes is rising much more rapidly due to increasing obesity and reduced physical activity levels as countries become more industrialized.

Diabetes leads to impaired carbohydrate metabolism in association with derangement in lipid metabolism, virtually every lipid, and lipoprotein is affected in Type 2 DM. Elevated triglycerides (TG) associated with low high-density lipoprotein cholesterol (HDL-C) levels, the preponderance of small dense lipoproteins and increased apolipoprotein B in diabetics is the most prevalent pattern of dyslipidemia.

While fasting hypertriglyceridemia may be an independent risk factor for atherosclerosis, particularly in the presence of DM, this the association has not been consistent and fasting HDL-C appears to be a far more significant risk factor for atherosclerosis.

Diabetic patients are frequently hyperlipidemic (approximately 70% of diabetic patients are dyslipidemic)

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and are at a higher risk for coronary heart disease due to atherosclerosis that accounts for approximately 80% of all mortality caused by diabetes and for most of the hospitalizations necessitated by complications of diabetes. The major risk factors contributing to an excess of cardiovascular disease caused by diabetes include hyperglycemia, insulin resistance, dyslipidemia, hypertension, smoking, albuminuria, and pro-coagulant state Type 2 diabetes is associated with the development of premature atherosclerosis. Diabetic dyslipidemia is believed to play an important role in the pathogenesis of accelerated atherosclerosis. The most important components of this dyslipidemia are elevated very low-density lipoproteins (VLDL), total TG, and a decreased HDL concentration in the serum. Several studies have proved that in type 2 diabetes, elevated TG levels may be a better predictor of ischemic heart disease (IHD) than elevated LDL cholesterol levels. Fasting hypertriglyceridemia has been consistently shown to be associated with a greater risk for coronary artery disease and atherosclerosis in those with Type 2 diabetes. It is now increasingly being recognized that atherosclerosis is a postprandial phenomenon. Serum TGs are generally increased maximally 3–6 h after a meal, particularly in diabetics. Once post-prandial hypertriglyceridemia occurs, it is exacerbated by the next meal and persists for the entire day. The vascular tree is exposed to this postprandial metabolic milieu most of the time.

As type 2 diabetic patients have significant postprandial lipid abnormalities, increased risk of atherosclerosis among them might be related to higher postprandial lipemia; hence, in the present study the aim is to investigate post-prandial lipid abnormalities in type 2 diabetic patients with and without macro-vascular disease and establish their role as a risk factor for atherosclerosis.

Aims and Objectives of the Study

Estimation of fasting TG levels in patients with type 2 DM with and without macrovascular complications. Estimation of post-prandial TG levels after an oral fat challenge in patients with type 2 DM with and without macrovascular complications. Compare post-prandial triglyceridemia with already established independent markers such as fasting TGs and HDL-C to establish post-prandial TG levels as an independent risk factor for atherosclerosis.

MATERIALS AND METHODS

This case–control study was done at SVS Medical College and Hospital, Mahbubnagar, between 2012 and 2014. In the present study, 75 patients between the age group of 30 and 65 years were selected, 50 patients with known diabetes were grouped as cases and 25 healthy patients without any coincidental illness were selected as controls. The cases were sub divided into two groups based on the history of macrovascular complications. Group I comprises patients with type 2 DM with history of macrovascular complications such as IHD and cerebrovascular disease (CVD), Group II comprises patients with Type 2 DM, of >1 year duration without evidence of IHD, CVD and peripheral vascular disease, and Group III comprises normal healthy age- and sex-matched patients without any history of diabetes, or any evidence of risk factors.

The diagnosis of DM was based on the recommendations of International Expert Committee that included representatives of the American Diabetes Association, the International Diabetes Federation, and the European Association for the Study of diabetes. The patients of type 2 DM >1 year duration were included in the study.

Inclusion Criteria: Cases

The following criteria were included in the study:

1. Patients with type 2 DM who visited the OPD or admitted in the hospital were selected.
2. Aged around 30–65 years.
3. Duration of diabetes >1 year.
4. Type 2 DM admitted with myocardial infarction or cerebrovascular events.
5. Type 2 DM with a history of myocardial infarction or cerebrovascular events on treatment.
6. Type 2 DM on treatment but without any history of treatment or admission for any IHD or cerebrovascular events were included in Group II.

Inclusion Criteria: Controls

The following criteria were included in the study:

1. 25 normal healthy patients were selected as controls.
2. Aged around 30–65 years.
3. There was no previous history of hypertension.
4. There was no previous history of Type 2 DM.
5. There was no evidence of any micro or macrovascular complications in the past.

Exclusion Criteria

The following criteria were excluded from the study:

1. Those patients who are <30 years and patients >65 years.
2. Those patients with evidence of nephropathy, retinopathy, and peripheral vascular disease
3. Those patients who are known diabetic for <1 year.
4. Those patients with history of smoking or alcoholism.

RESULTS [TABLES 1-5]

The present study was undertaken in the Department of General Medicine, S.V.S Medical College and Hospital, Mahabubnagar.

Table 1: Distribution of subjects by age group

Age group in years	Group 1: Diabetes with complication	Group 2: Diabetes without complication	Group 3: Controls
	n (%)	*n* (%)	*n* (%)
30–40	9 (36)	9 (36)	8 (32)
41–50	8 (32)	7 (28)	10 (40)
51–60	7 (28)	8 (32)	6 (24)
61–70	1 (4)	1 (4)	1 (4)
Total	25 (100)	25 (100)	25 (100)
Mean±SD	45.16±9.4	45±10.8	45.6±9.34
Range	30–61	30–62	30–63

F=0.25, *P*=0.97. SD: Standard deviation

Table 2: Sex-wise distribution of subjects among three groups

Sex	Group 1: Diabetes with complication	Group 2: Diabetes without complication	Group 3: Controls
	n (%)	*n* (%)	*n* (%)
Male	17 (68)	16 (64)	17 (68)
Female	8 (32)	9 (36)	8 (32)
Total	25 (100)	25 (100)	25 (100)

χ^2=0.12, *P*=0.947

Table 3: Distribution of subjects based on duration of diabetes

Duration of DM years	Group 1: Diabetes with complication	Group 2: Diabetes without complication
	n (%)	*n* (%)
1–5	3 (12)	17 (68)
6–10	18 (72)	8 (32)
11–15	4 (16)	0 (0)
Total	25 (100)	25 (100)
Mean±SD	8.28±2.37	3.5±1.7

DM: Diabetes mellitus

Table 4: Distribution of subjects based on treatment

Rx	Group 1: Diabetes with complication	Group 2: Diabetes without complication
	n (%)	*n* (%)
OHA	11 (44)	18 (72)
Insulin	7 (28)	5 (20)
Both	7 (28)	2 (8)
Total	25 (100)	25 (100)

χ2=4.81, *P*=0.09

A total of 75 age-, sex-, and body mass index (BMI)-matched subjects were recruited from S.V.S Medical College and Hospital for the present study, of which 25 subjects constituted the control group called as Group 3 and remaining 50 subjects constituted the case group which was subdivided into two groups: Group 1 comprised 25 subjects with a history of diabetes and macro vascular complication and Group 2 comprised 25 subjects with a history of diabetes without macrovascular complication.

The following parameters were analyzed.

- Fasting blood glucose
- Post-prandial blood glucose
- Blood urea
- Serum creatinine
- Total cholesterol
- Fasting TGs
- LDL cholesterol
- HDL-C
- VLDL
- Serum TG (after an oral fat challenge).

The results were expressed in mg/dl for glucose, urea, creatinine, total cholesterol, HDL, LDL, VLDL, and TG.

The data were analyzed using SPSS software version 17.0. Descriptive results are expressed as mean and SD of various parameters in different groups, multiple comparisons ANOVA was used to assess the significance of the difference of mean values of different parameters in between control, groups, diabetes without complication, and diabetes with complication. F value was used to calculate the significance in between groups.

The age of the patients varied form a minimum age of 30 years to a maximum of 63 years. The mean age of the patients in the three groups was not significantly different from each other F = 0.25, $P > 0.05$.

Among the total 50 patients, 33 were males (66%) and 17 were females (34%).

In Group 1 of the 25 patients, 17 were males (68%) and 8 were females (32%).

In Group 2 of the 25 patients, 16 were males (64%) and 9 were females (36%).

Table 5: Distribution of subjects according to the BMI in different groups

BMI	Group 1: Diabetes with complication	Group 2: Diabetes without complication	Group 3: Controls
	n (%)	*n* (%)	*n* (%)
21–25	10 (40)	12 (48)	18 (72)
26–30	1 (56)	12 (48)	7 (28)
31–35	1 (4)	1 (4)	0 (0)
Total	25 (100)	25 (100)	25 (100)
Mean±SD	26.2±2.42	25.92±2.76	24.4±2.25
Range	21–31	21–31	21–39

F=3.829, *P*=0.026. BMI: Body mass index

In Group 3 of the 25 patients, 17 were males (68%) and 8 were females (32%).

There was no significant difference observed in the sex distribution of subjects among the three groups; Chi-square value was 0.12 and significance $P > 0.05$.

In Group 1, 11 patients were in OHA (44%), and 7 patients were on insulin (28%), whereas 7 patients (28%) received both insulin and OHA together. In Group 2, 18 patients were in OHA (72%), and 5 patients were on insulin (20%), whereas 2 patients (8%) received both insulin and OHA together. There was no significant difference observed in the mode of treatment Chi-square value 4.81, and significance $P > 0.05$.

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 ($P = 0.118$) and Group 2 and Group 1($P = 0.878$).

The mean values for FBS, PPBS, total cholesterol, creatinine, and post-meal TGs are significantly higher in diabetes with complication group compared to diabetes without complication and controls.

The mean values of fasting TGs, LDL, and VLDL were not significantly higher in diabetes with complication group compared to diabetes without complication.

The mean value of HDL was not significantly lower in diabetes with complication group compared to diabetes without complication.

The mean values for FBS, PPBS, total cholesterol, creatinine, VLDL, and post-meal TGs are significantly higher in diabetes without complication group compared to controls, whereas HDL values were significantly lower in diabetes without complication group compared to controls as shown in Table 6-8.

In Group 1, 7 patients (28%) had suffered from MI as the complication, 8 patients (32%) had suffered from cerebrovascular accident (CVA) as the complication, and 10 patients (40%) had suffered from both MI and CVA as the complication.

To assess the maximum sensitivity, specificity, and diagnostic efficiency of TGs in identifying abnormality, the best cutoff values are calculated using ROC analysis. Best cutoff 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 9. 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 cutoff values for different parameters along with sensitivity, specificity, and diagnostic efficiency values for Group 1 and Group 2 are presented in Table 10.

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

DISCUSSION

DM is the most common metabolic disorder, a social and economic burden to the society due to the increased morbidity and mortality associated with its complications.[1]

Macrovascular disease is a major cause of death in diabetic individuals.

Since many diabetic individuals have multiple risk factors for atherosclerosis, the relative risks of IHD and CVD are 2–4-fold and 2–3-fold higher, respectively, than the risk in nondiabetic subjects.[2]

Table 6: Mean±SD values of studied parameters in diabetes with complication, diabetes without complication and controls

Parameter	Group 1: Diabetes with complication	Group 2: Diabetes without complication	Group 3: Controls
	Mean±SD	Mean±SD	Mean±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

SD: Standard deviation, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoproteins

Table 7: F, *P* value of various parameters between cases and controls

Parameter	F value	*P* value
FBS	45.9	<0.001
PPBS	46.9	<0.001
Urea	3.18	0.047
Creatinine	12.6	<0.001
Total cholesterol	12.58	<0.001
Triglyceride fasting	25.13	<0.001
HDL	33.77	<0.001
LDL	9.53	<0.001
VLDL	25.06	<0.001
Triglyceride post fat meal	36.519	<0.001

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoproteins

Table 8: ANOVA multiple comparision of significance

Parameter	Group 1		Group 2
	Group 2	Group 3	Group 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

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoproteins

In the present study, the mean age group in the controls was 45.6 years, in diabetic patients without complication 45 years and diabetic patients with complication 45.16 years.

In a study done by Kumar *et al*.: On evaluation of Post-Prandial hyper triglyceridemia in Patients with Type 2 DM with and without macrovascular disease, have shown that the mean age group in the controls was 51.1 years, in diabetic patients without complication 54.6 years and in diabetic patients with complication 54.5 years respectively.

Table 9: Distribution of subjects based on complication in Group 1

Complication	Group 1: Diabetes with complication
	n (%)
MI	7 (28)
CVA	8 (32)
Both	10 (40)
Total	25 (100)

CVA: Cerebrovascular accident

Summary

A prospective study of 75,sex,BMI matched patients,in this 50 patients are cases in this two groups are there group 1 is TYPE 2 DM with macrovascular complications and group 2 is TYPE 2 DM without any macrovascular complications and remaining 25 were controls this is group 3 without DM was done in Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal Dist., Telangana State. The inclusion and exclusion criteria were followed according to the criteria's mentioned in the materials and methods.

1. The age range of the patient was 30–63 years, with male and female ratio in Group 1 is 2.125:1, in Group 2 is 1.77:1, and in Group 3 is 2.125:1.
2. Duration of diabetes in Group 1 is around 8.28 years, in Group 2 is 3.5 years.
3. Among the cases 44% of Group 1 and 72% of Group 2 on OHA'S, 28% of Group 1 and 20% of Group 2 on insulin, 28% of Group 1 and 8% of Group 2 taking both medications.
4. Fasting blood sugars in Group 1; 205.2 mg/dl, Group 2; 150.6 mg/dl, and Group 3 85.1 mg/dl, fasting TGs in Group 1; 223.43 mg/dl, Group 2; 199.6 mg/dl, and Group 3; 126.08 mg/dl.
5. Post-prandial blood sugars in Group 1; 294.68 mg/dl, Group 2; 204 mg/dl, and Group 3 114.6 mg/dl, post-prandial TGs after fat meal in Group 1; 407.2 mg/dl, Group 2 337.6 mg/dl, and Group 3; 211.3 mg/dl.

Table 10: Best cutoff values, diagnostic efficiency, sensitivity, specificity, in discriminating diabetes with complication and diabetes without complication

Parameter	Best cut off values	Sensitivity (%)	Specificity (%)	Diagnostic efficiency (%)
Duration of diabetes	6.5 years	80	84	82
Triglycerides fasting	167.5 mg/dl	88	40	64
Triglycerides post fat meal	328.5 mg/dl	80	60	70

6. In Group 1; 28% of patients having MI, 32% of patients having CVA, and 40% having both.

CONCLUSION

1. Macrovascular complications are more commonly observed in Type 2 DM.
2. Chief observation in the present study was that elevated fasting TG level was significantly associated in patients with diabetes. However, the more higher association was observed in this study between elevated post-prandial TG level and patients with diabetes and macrovascular complication.
3. Post-prandial hypertriglyceridemia, in addition to fasting hypertriglyceride levels, may be an independent risk factor for early atherosclerosis in type 2 diabetes.
4. Evaluating not only FTG level but also PPTG level during clinical assessment of patients with type2 diabetes is important as PPTG was observed to have higher diagnostic efficiency compared to FTG levels.

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