

Post prandial lipid abnormalities in type 2 diabetes mellitus

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Abstract

It is increasingly believed that atherosclerosis is a postprandial phenomenon; high postprandial triglycerides have shown a strong independent association with CAD. Therefore measurement of lipids especially triglycerides in postprandial state would be more reliable and sensible indicator to predict future cardiovascular risk.

This study was done in 50 patients with Type 2 Diabetes Mellitus and 50 age, sex and BMI matched healthy controls. Patients were on usual dose of oral hypoglycemic agents or insulin. Preliminary clinical and laboratory assessment was done in diabetic subjects and controls.

After a 12 hrs over night fast standardized meal providing 600 kcals., was given to all subjects. Blood was drawn after 4hrs for measurement of lipid profile. The fasting lipid profile in type 2 diabetes mellitus differed from controls only in a significantly lower HDL value. There was no significant difference in any other lipid parameters.

Significant postprandial lipid abnormalities were observed in the diabetic subjects particularly triglycerides (P=0.0001). Postprandial hypertriglyceridemia was directly correlated with BMI and glycaemic control. Postprandial hypertriglyceridemia was not correlated with age of the patient and duration of diabetes.

Keywords: Type 2 Diabetes, Triglycerides, Coronary Artery Disease (Cad)

Introduction

Worldwide prevalence of diabetes has risen dramatically over the past two decades. The marked increase in the growth of diabetes population is due to rapid changes in life style following urbanization, lack of physical exercise and dietary habits.

Type 2 Diabetes mellitus is associated with the development of premature atherosclerosis and a higher cardiovascular morbidity and mortality [1]. Patients with type 2 diabetes mellitus have a 3 to 4 fold higher risk for cardiovascular disease than non-diabetic persons [2]. Diabetic dyslipidaemia is believed to play an important role in the Pathogenesis of accelerated atherosclerosis in this condition [3].

The Predominant lipid abnormalities seen in diabetes mellitus are elevated serum Triglyceride level and low HDL cholesterol level and an increase in the proportion of small dense LDL [2].

Both World Health Organization (WHO) multinational trial & Paris Prospective study have shown that hypertriglyceridemia is a significant predictor of subsequent cardio vascular mortality in patients with diabetes [2, 4].

In Stockholm Ischemic heart disease secondary prevention study, lowering triglyceride levels was the most important factor in decreasing total cardiovascular mortality [5].

It is being increasingly believed that atherogenesis is a postprandial phenomenon as at least with respect to lipids, as we are in the postprandial phase for most of the day. High postprandial triglycerides have shown a strong independent association with CAD [6].

Aims & Objectives

1. To study the postprandial lipid abnormalities in type 2 Diabetes Mellitus.

2. To compare postprandial lipid profiles in Diabetics and Controls.

Material & Methods

Inclusion Criteria

50 Patients with Type - 2 Diabetes Mellitus and 50 age and sex matched healthy controls
Diabetes diagnosed according to ADA Criteria. (FBS \geq 126 mg /dl, PLBS \geq 200mg/dl. Patients were on usual dose of insulin or oral hypoglycemic drugs.

Exclusion Criteria

1. Familial Hyperlipidaemia
2. Nephropathy
3. Hepatic disease
4. Hypothyroidism
5. Cushing Disease
6. Alcoholism
7. List of Drugs affecting Lipids (anti hyperlipidaemic agents, Beta blockers, Thiazide Diuretics.
8. Fasting triglycerides > 250mg/dl.

Preliminary Clinical & Lab assessment done in both diabetic subjects & Controls. These included.

- Fasting and postprandial Blood Sugar (FBS), (PLBS)
- Glycosylated Haemoglobin (HbA_{1c})
- Lipid Profile (Fasting)
- Kidney & Liver Function tests.
- Thyroid Profile
- ECG, X - Ray chest.

After a 12 hrs over night fast, a standardized meal was given to all subjects. Providing 600K.cal. Consisting 60%

Carbohydrates, 20 - 25 % Proteins, 15 - 20% Fats - 3 pulka, 1½ cup rice, 1cup of Vegetable curry, 1cup of sambar, 1 cup of curd.

Blood was collected in fasting and 4hrs after meal for lipid profile measurements.

Freidwald formula

$$LDL-C = TC - HDL-C - (TRIGLYCERIDE/5)$$

Observation & Results

Table 1: Distribution of male and female subjects

	Diabetes	Controls
Male	32 (64%)	32 (64 %)
Female	18 (36%)	18 (36%)

Table 2: Age Distribution

AGe	Diabetes	Controls
40 - 44	2 (4%)	2 (4 %)
45 - 49	8 (16%)	8 (16%)
50 - 54	13 (26%)	13 (26%)
54 - 59	27 (54%)	27 (54%)

Age in Diabetics	Postprandial triglycerides (Mean)
40 - 44	157 mg/dl
45 - 49	182.37 mg/dl
50 - 54	194.07 mg/dl
55 - 59	194.07 mg/dl

There was no correlation between age of the patients and postprandial triglycerides. $r = 0.228, P = 0.111 (> 0.05)$

Table 3: Duration of Diabetes

Duration	Number(Percentage)
< 5	16 (32%)
5 - 10	25 (50%)
> 10	9 (18%)

Duration of diabetes	Postprandial triglycerides (Mean) in diabetics
< 5 yrs.	179.25 mg/dl
5 - 10 yrs.	194.32 mg/dl
> 10 yrs.	192.8 mg/dl

There was no correlation between duration of diabetes and postprandial triglycerides. $r = 0.180, P = 0.210 (> 0.05)$

Table 4: Incidence of obesity in subjects with diabetes and controls

	Bmi	Diabetes	controls
Obese	≥ 30	16 (32%)	16 (32%)
Over Weight	25 - 29.9	18 (36%)	18 (36%)
Non Obese	< 25	16 (32%)	16 (32%)

Of the 50 Diabetic subjects 16 (32%) are obese, 18 (36%) are overweight and 16 (32%) are non-obese.

Postprandial triglycerides in relation to BMI

BMI	Postprandial triglycerides (Mean) in diabetics
< 25	172.93 mg/dl
25 - 29.9	198 mg/dl
> 30	201.8 mg/dl

There was direct correlation between BMI of the patients and postprandial triglycerides. $r = 0.377, P = 0.007 (< 0.05)$

Table 5: Glycaemic control in cases of diabetes

HbA1C	No of diabetic patients
< 7	14 (28%)
7 - 8	24 (48%)
> 8	12 (24%)

There was direct correlation between HbA1C and postprandial triglycerides.

Table 6: Incidence of Coronary Artery Disease

	Diabetics	Controls
CAD	16 (32%)	5 (10%)

Significant no of diabetics has Coronary Artery Disease. ($P < 0.05$)

Table 7: Fasting Total Cholesterol Levels

Fasting Total Cholesterol Levels	No. of Diabetics	No. of controls
> 200 mg/dl	22 (44%)	17 (34%)
≤ 200 mg/dl	28 (56%)	33 (66%)

There was no significant difference in fasting Cholesterol levels among the patients and Controls. ($P < 0.34$)

Postprandial Total Cholesterol Levels

Postprandial Total Cholesterol Levels	No. of Diabetics	No. of controls
> 200 mg/dl	24 (48%)	20 (40%)
≤ 200 mg/dl	26 (52%)	30 (60%)

There was no significant difference in Postprandial Cholesterol levels among the patients and Controls. ($P < 0.2$)

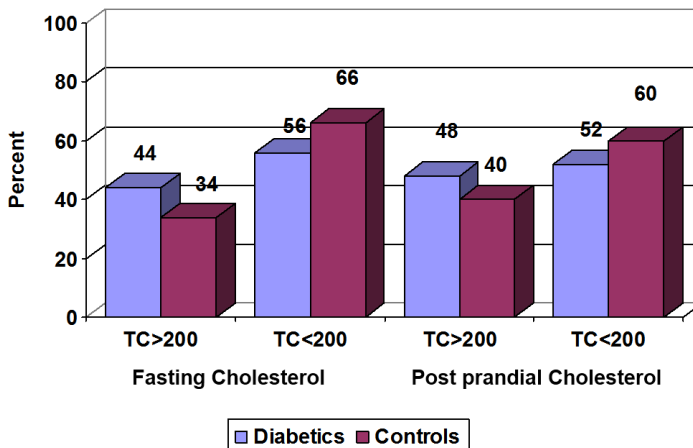


Table 8: Fasting HDL Levels

Fasting HDL	No. of Diabetics	No. of controls
> 40 mg/dl	21 (42%)	30 (60%)
≤ 40 mg/dl	29 (58%)	20 (40%)

There was significant difference in fasting HDL Cholesterol among the patients and Controls. ($P = 0.013$)

Postprandial HDL levels

Postprandial HDL	No. of Diabetics	No. of controls
> 40 mg/dl	19 (38%)	33 (66%)
≤ 40 mg/dl	31 (62%)	17 (34%)

There was significant difference in postprandial cholesterol among the patients and Controls. ($P = 0.001$)

HDL

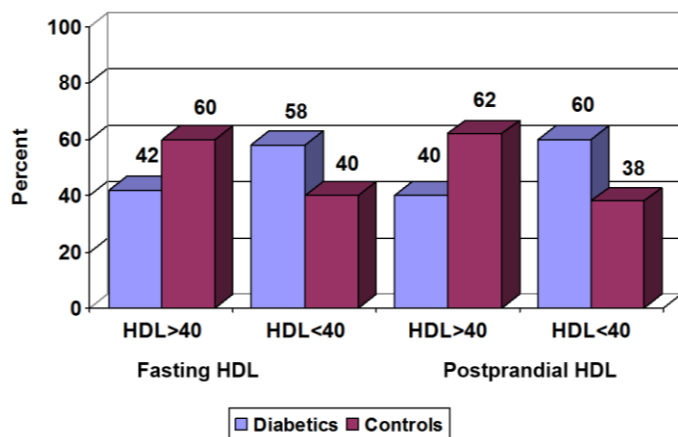


Table 9: Fasting LDL Levels

Fasting LDL Levels	No. of Diabetics	No. of controls
> 100 mg/dl	32 (64%)	26 (52%)
≤ 100mg/dl	18 (36%)	24 (48%)

There was no significant difference in fasting LDL among the patients and Controls. (P - 0.31)

Postprandial LDL Levels

Postprandial LDL Levels	No. of Diabetics	No. of controls
> 100 mg/dl	36 (72%)	32 (64%)
≤ 100mg/dl	14 (28%)	18 (36%)

There was no significant difference in Postprandial LDL among the patients and Controls. (P. 0.15)

LDL

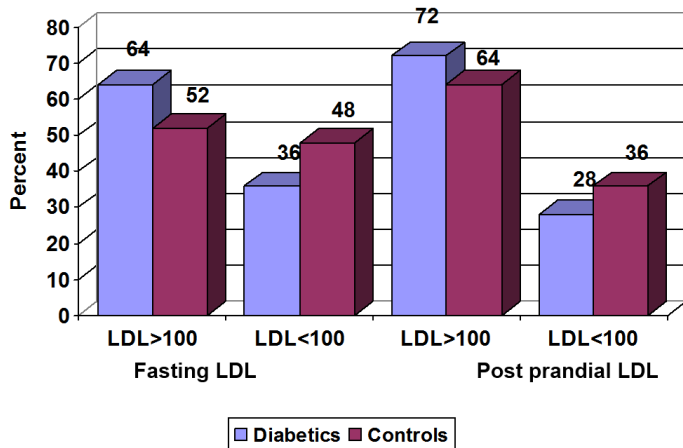


Table 10: Fasting Triglyceride Levels

Fasting Triglycerides	No. of Diabetics	No. of controls
> 150 mg/dl	31(62%)	30(60%)
≤ 150mg/dl	19(38%)	20(40%)

There was no significant difference in Fasting Triglyceride levels among the patients and Controls. (P. 0.15)

Postprandial Triglyceride Levels

Postprandial Triglycerides	No. of Diabetics	No. of controls
> 200 mg/dl	31 (62%)	7 (14%)
≤ 200mg/dl	19 (38%)	43 (86%)

There was significant difference in Postprandial Triglyceride levels among the patients and Controls. (P- 0.0001)

Triglycerides

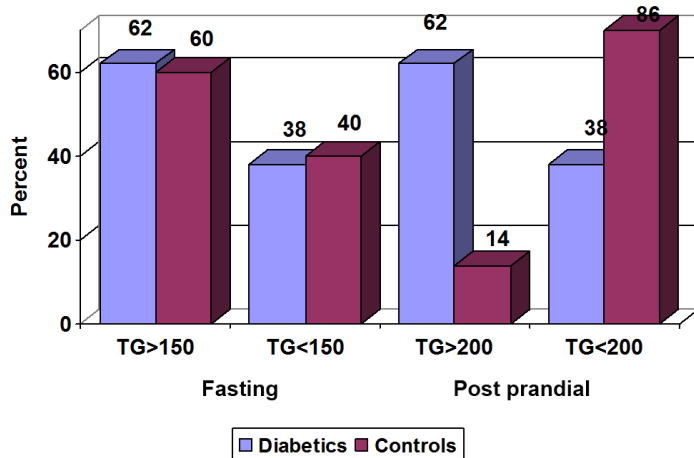


Table 11: Fasting VLDL Levels

Fasting VLDL	No. of Diabetics	No. of controls
> 30 mg/dl	25(50%)	23(46%)
≤ 30mg/dl	25(50%)	27(54%)

There was no significant difference in Fasting VLDL levels among the patients and Controls. (P - 0.96)

Postprandial VLDL Levels

Postprandial VLDL	No. of Diabetics	No. of controls
> 30 mg/dl	39 (78%)	36 (72%)
≤ 30mg/dl	11 (22%)	14 (28%)

There was significant difference in Postprandial VLDL levels among the patients and Controls. (P. 0.0003).

Discussion

It is increasingly believed that atherogenesis is a postprandial phenomenon at least with respect to lipids as postprandial phase is common most of the day. High postprandial triglycerides have shown a strong independent association with CAD. This study was done to identify the post prandial lipid profile status in diabetic subjects.

This study was conducted in 100 cases who attended in General Medicine and Endocrinology Departments of Osmania General Hospital.

Out of the 100 cases 50 were diabetics, and 50 served as controls. In this study among 50 cases of type 2 diabetes, 32 were males and 18 were females. In control group also males and females were same in number. Majority of the diabetes were in age group between 55 to 59. This indicates that as the age increases, incidence of type 2 diabetes is also increased. In 50 cases of type 2 diabetes mellitus 32% were obese 36% were over weight and 32% were non obese. Majority of the diabetics were overweight & obese. Among 50 diabetic patients, majority of patients (72%) had HbA1c above 7.

The mean fasting triglyceride levels in diabetics and controls were similar. There was no statistically significant difference (p:0.15) between the two groups. In contrast there was a statistically significant difference in mean triglyceride levels between diabetics and controls in post prandial state. (p:0.001) Obesity and Postprandial Triglycerides: In our study obese and over weight individuals had higher levels of postprandial triglycerides compared to diabetics with normal BMI. Obesity

appears to influence postprandial triglyceride levels in type 2 DM, as high postprandial triglyceride levels showed direct correlation with BMI.

There was direct correlation between BMI of the patients and postprandial triglycerides. $r = 0.377$, $P = 0.007$

Glycaemic Control and Postprandial Triglycerides: In our study Postprandial triglyceride levels were directly correlated with HbA_{1C} levels. Higher the HbA_{1C} greater the postprandial triglyceride levels.

There was no correlation between age of the patients and postprandial triglycerides. $r = 0.228$; $P = 0.111$

There was no correlation between duration of diabetes and postprandial triglycerides. $r = 0.180$, $P = 0.210$.

Two manuscripts published in the Journal of the American Medical Association address the importance of post prandial hyper triglyceridemia by comparing fasting with postprandial triglycerides with respect to the prediction of future cardiovascular events. In the first report derived from the Women's Health Study cohort, both fasting and postprandial triglycerides were associated with future cardiovascular risk after adjustments were made for age, blood pressure, smoking status, and hormone-replacement therapy. Postprandial triglycerides maintained a strong independent relationship with future cardio vascular events in fully adjusted analyses. Moreover, in analyses stratified by time since the last meal, triglyceride concentrations measured 4 h post prandially had the strongest association with cardiovascular events [7].

The second report derived from a prospective cohort of 7,587 women and 6,394 men in Copenhagen with 26 years of follow-up [8]. In this study, postprandial triglycerides were also found to significantly predict future vascular events in both sexes after multivariate analysis. The highest risks were observed among the individuals with the very highest postprandial triglyceride concentrations (≥ 5 mmol/L).

There was no statistically significant difference in total cholesterol, LDL cholesterol levels among diabetics and controls in the fasting state. ($p:0.31$). Post prandially also, there was no statistically significant difference in mean total cholesterol and LDL cholesterol levels among the two groups studied. ($p:0.15$).

Among diabetics 42% diabetics had fasting HDL > 40 mg/dl. Among controls 60% had fasting HDL > 40 mg/dl. There was significant difference in fasting HDL Cholesterol among the patients and Controls. ($P 0.013$).

Among diabetics only 38% patients had Postprandial HDL > 40 mg/dl

Among controls 66% had postprandial HDL > 40 . There was significant difference in postprandial HDL cholesterol among the patients and Controls. ($P 0.001$).

In a study by madhu *et al* [9], fasting lipid profile in type 2 diabetic patients differed from controls only in a significantly lower HDL cholesterol value. There was no significant difference in any of the other lipid parameters in the fasting state. Significant post prandial lipid abnormalities were observed in the diabetic subjects particularly triglycerides and HDL. Post prandial triglyceride levels showed significant correlation with BMI and fasting triglyceride values [3, 8]. The results of our study are in accordance with the findings of the above study.

In another study by sumesh raj *et al* [10], there was no significant difference in fasting HDL, LDL and triglyceride

levels between diabetics and controls. The lipid profile showed significantly higher levels of total cholesterol and post prandial triglycerides. ($p<0.01$) in diabetics compared to the controls. post prandial hypertriglyceridaemia directly correlated with BMI and glycaemic control. There was no correlation between postprandial triglyceride levels with age and duration of diabetes. In our study there was significant difference in HDL levels between fasting and post prandial states among patients and controls. In our study also there was a significant increase in post prandial triglyceride levels among diabetics.

High postprandial triglyceride level were present in diabetics when compare to control group despite similar fasting triglyceride levels. It shows that at least in diabetic subjects estimating lipids in postprandial phase is far more important than in fasting stage.

It is not very clear whether it is the fasting triglyceride levels which determines postprandial triglyceride level or postprandial triglyceride level that determine the Fasting triglyceride level. It would appear that it is the postprandial triglyceride level that determine the fasting triglyceride levels. Postprandial triglyceride level peaks at 6 – 8 hr. after meals and remains higher after attaining the peak in most of the period. So fasting triglyceride levels estimated 12 – 14 hrs. after previous meals would thus represent the down slop of Postprandial triglyceride levels. So, Postprandial triglyceride measurement in diabetics is more reasonable than fasting triglyceride levels, as fasting triglyceride is mere reflection down slop of Postprandial triglyceride level.

Despite the growing literature the precise cut off point for postprandial hyper lipidemia is not yet known several studies shows increase in more than 15% postprandial triglycerides from fasting state as cut off point [11].

It may be rational to investigate for postprandial lipids in those with normal fasting lipid levels but having abdominal obesity and metabolic syndrome in Asian Indians [12, 13].

Further studies are required regarding routine measurements of postprandial triglycerides and treatment options for postprandial hypertriglyceridemia.

limitations of the study

- The major limitation of the study is that, it was done in a small group and this may not represent the entire population.
- We adjusted for major confounders, but as with all observational studies, the possibility of residual confounding might affect the results.

Conclusions

1. Significant postprandial lipid abnormalities in type 2 diabetes.
2. Significant increase in postprandial triglycerides in diabetics when compare to controls.
3. Postprandial hyper triglyceridemia is directly correlated with BMI and HbA_{1C}
4. No significant difference in fasting triglycerides levels in cases and controls.
5. No correlation between postprandial hypertriglyceridemia with age and duration of diabetes.

References

1. Garcia MJ, Mc Namara PM, Gordon T, Kannel WB. Morbidity and mortality in diabetics in the Framingham population, Sixteen year follow-up study. *Diabetes* 1974; 23:105-11.
2. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects. *N Engl J Med.* 1998; 339:229-34.
3. Fontbonne A. Relationship between diabetic dyslipoproteinemia and coronary heart disease risk in non-insulin dependent diabetes. *Diabetes Metab Rev* 1991; 7:179-89.
4. West KM, Ahuja MMS, Bennet PH, Czyzyk A, DeA costa OMD, Fuller JH *et al.* Role of circulating glucose & triglyceride concentrations and their interaction with other risk factors as determinants of arterial disease in nine diabetic population samples from the WHO Multicenter Study. *Diabetes Care* 1983; 6:361-69.
5. Carlson LA, Rosenhamer G. Reduction of mortality in the Stockholm ischemic heart disease secondary prevention study by combined treatment with clofibrate and nicotinic acid.
6. Zilversmit DB. Atherosclerosis: a postprandial phenomenon. *Circulation* 1979; 60:472-85.
7. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with post prandial triglycerides and risk of cardiovascular events in women. *JAMA.* 2007; 298:309-316.
8. Ordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. Post prandial triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA.* 2007; 298:299-308.
9. Postprandial lipid abnormalities in type 2 diabetes mellitus – S.V.Madhu *et al.*, - *Journal of the Association of Physicians of India.* 2005, 53.
10. Postprandial hypertriglyceridemia in type 2 diabetics subjects. Sumesh Raj, C. Rajshekar, B. Jayakumar - *International Journal of Diabetes in Developing Countries* year. 2006; 26(4):160-162
11. Snehalatha C, Sivasankari S, Satyavani K, Vijay V, Ramachandran A. Postprandial hypertriglyceridaemia in treated type 2 diabetic subjects - the role of dietary components. *Diabetes Res Clin Pract* 2000; 48:57-60.
12. Misra A, Vikram NK. Clinical and pathophysiological consequences of abdominal adiposity and abdominal adipose tissue depots. *Nutrition* 2003; 19:457-66.
13. Couillard C, Bergeron N, Prud'homme D, Bergeron J, Tremblay A, Bouchard C *et al.* Postprandial triglyceride response in visceral obesity in men. *Diabetes* 1998; 47:953-60.