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## Original Research Article

## Study to find out the significance of postprandial dyslipidemia in diabetic patients

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## ABSTRACT

**Introduction:** Diabetes Mellitus (DM) is a group of metabolic diseases, which is characterized by chronic hyperglycaemia, which results from the defects in the insulin action, insulin secretion or both. The most prevalent form of the disease, type 2 Diabetes Mellitus is often asymptomatic in the early stages and it may remain undiagnosed for many years. The insulin resistance in the liver leads to failure of the hyperinsulinaemia to suppress the gluconeogenesis, which increases fasting glucose levels and decreases glycogen storage by the liver in the postprandial phase. Increased glucose production in the liver occurs early in the course of diabetes, and it is likely in skeletal muscles after the onset of the insulin secretory abnormalities and the insulin resistance. Due to the insulin resistance in the adipose tissue and obesity, the free fatty acid (FFA) flux from the adipocytes is increased, which in turn leads to an increase in lipid [very low-density lipoprotein (VLDL) and triglycerides] synthesis in the hepatocytes. This is responsible for the dyslipidaemia which is found in type 2 diabetes mellitus [elevated triglycerides, reduced HDL, and increased low-density lipoprotein (LDL) particles: Individuals with type 2 diabetes mellitus are at increased risk of developing microvascular and macrovascular complications.

**Objective:** To find out the significance of postprandial dyslipidemia in diabetic patients.

**Materials and Methods:** This is a cross-sectional study, wherein written informed consent was taken after giving detailed information to the participants regarding the study. Patients who were in the age group of 35-65 years, admitted in the Department of Medicine, RRMCH from November 2017 for next 18 months with Diabetes Mellitus who met a predefined inclusion and exclusion criteria were studied. The study was initiated after obtaining clearance from the institution's ethical committee.

**Results:** There was a significant elevation of mean values of total serum cholesterol, LDL and TG of cases and controls in the postprandial state compared to their fasting state, statistical significance was found ( $P < 0.05$ ). Mean values of total serum cholesterol, LDL and TG of cases in fasting state were significantly more compared to controls in fasting state, statistical significance was found ( $P < 0.05$ ). Mean values of total serum cholesterol, LDL and TG of cases in the postprandial state were significantly more compared to controls in the postprandial state, statistical significance was found ( $P < 0.05$ ). Mean values of both FBS and PPBS in cases were higher compared to controls ( $P < 0.05$ ). Mean values of PPBS in cases and controls were significantly more compared to their respective FBS values ( $P < 0.05$ ). The mean HbA1c values in cases were higher (7.142) compared to controls (5.554).

**Conclusion:** Prevalence of diabetes was highest in the age group 56-65 years in our hospital. As the duration of diabetes increases, there is an increased prevalence of dyslipidemia in the cases. Past history of HTN, IHD, PVD and CVA were found significantly more in subjects with fasting and postprandial dyslipidemia (cases) compared to those without (controls). Patients on irregular treatment (63%) were more in the study group (cases) compared to controls. So it could be said that patient not on regular treatment are more prone to have dyslipidemia. (fasting as well as postprandial). There was a significant increase in total serum cholesterol, LDL and TG in postprandial states of cases compared to that in controls, so it could be said that diabetic patients with fasting dyslipidemia are more prone to have dyslipidemia in the postprandial state.

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## 1. Introduction

Diabetes Mellitus (DM) is a group of metabolic diseases, which is characterized by chronic hyperglycaemia, which results from the defects in the insulin action, insulin secretion or both. The most prevalent form of the disease, type 2 Diabetes Mellitus is often asymptomatic in the early stages and it may remain undiagnosed for many years. The insulin resistance in the liver leads to failure of the hyperinsulinaemia to suppress the gluconeogenesis, which increases fasting glucose levels and decreases glycogen storage by the liver in the postprandial phase. Post prandial triglyceridemia is a distinct component of diabetic dyslipidemia.<sup>1,2</sup>

Atherosclerosis is a postprandial phenomenon with respect to lipids, as we are in the postprandial state for the most of the day.<sup>3</sup> Increased glucose production in the liver occurs early in the course of diabetes, and it is likely in skeletal muscles after the onset of the insulin secretory abnormalities and the insulin resistance.<sup>4</sup> Due to the insulin resistance in the adipose tissue and obesity, the free fatty acid (FFA) flux from the adipocytes is increased, which in turn leads to an increase in lipid (very low-density lipoprotein (VLDL) and triglycerides) synthesis in the hepatocytes. This is responsible for the dyslipidaemia which is found in type 2 diabetes mellitus [elevated triglycerides, reduced HDL, and increased low-density lipoprotein (LDL) particles]. Individuals with type 2 diabetes mellitus are at increased risk of developing microvascular and macrovascular complications.

Postprandial hyperglycemia is one of the earliest abnormalities of glucose homeostasis associated with type 2 diabetes mellitus and is markedly exaggerated in diabetic patients with fasting hyperglycemia.<sup>5–7</sup> Increased postprandial glucose (PPG) concentrations contribute to suboptimal glycemic control.

Postprandial hyperglycemia is one of the earliest abnormalities of glucose homeostasis associated with type 2 diabetes mellitus and is markedly exaggerated in diabetic patients with fasting hyperglycemia. The mechanisms by which acute hyperglycemia spikes exerts its effects may be attributed to the production of free radicals. This alarmingly suggestive evidence for harmful effects of postprandial hyperglycemia on diabetes complications has been sufficient to influence guidelines from important professional scientific societies. Correcting the postprandial hyperglycemia may form a key part of the strategy for the prevention and management of CVDs in diabetes.<sup>5–9</sup>

Increasing evidence from the recent studies suggests that the postprandial state is a major contributing factor to the development of complications like atherosclerosis. In type 2 diabetes, the postprandial phase is characterized by a large and rapid increase in the levels of blood glucose, and

the possibility that the postprandial "hyperglycemic spikes" may be relevant to the onset of cardiovascular complications has recently received much attention.

## 2. Objective of The Study

To find out the significance of postprandial dyslipidemia in diabetic patients

## 3. Material and Methods

This is a descriptive cross-sectional study, wherein written informed consent was taken after giving detailed information to the participants regarding the study. Patients who were in the age group of 35-65 years, admitted in the Department of Medicine, RRMCH from November 2017 for next 18 months with Diabetes Mellitus who met a predefined inclusion and exclusion criteria were studied. The study was initiated after obtaining clearance from the institution's ethical committee.

### 3.1. Inclusion criteria

All type 2 DM patients who were in the age group of 35-65 years on regular treatment with OHA which had a duration of diabetes of more than 5 years in medicine OPD, diabetic clinic and wards.

### 3.2. Exclusion criteria

1. Type I DM patients
2. Patients with congenital hyperlipidemia
3. Diabetic patient on the hypolipemic drug
4. Patients on insulin therapy
5. Gestational Diabetic patients
6. Patients with thyroid disease
7. Patients not willing for the study

### 3.3. Sample

50 cases of type 2 diabetes mellitus with abnormal fasting lipid profile (one or more lipid parameter) and 50 controls of type 2 diabetes mellitus with normal fasting lipid profile.

### 3.4. Operational definitions

1. Type 2 Diabetes mellitus patients were classified as having type 2 DM using clinical criteria such as a present/prior history of usage of OHAs or usage of a combination of insulin and the OHAs.

### 3.5. Diabetes is diagnosed by world health organization (WHO) criteria

1. Fasting plasma glucose (FPG)  $\geq 126$  mg/dl ( $\geq 7.0$  mmol/l) or,

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2. Oral glucose tolerance test (OGTT with fasting plasma glucose >126 mg/dl (7.0
3. Mmol/l and/or 2 hours plasma glucose >200 mg/dl (11.1 mmol/l or,
4. Glycated hemoglobin (HbA1c > 6.5 mg/dl or 48 mmol/mol, or
5. Random plasma glucose >200 mg/dl (11.1 mmol/l in the presence of classical diabetes symptom

- Plasma glucose is measured by Randox autoanalyser using the colorimetric method without deproteinisation using glucose oxidase enzyme.
- Dyslipidaemia: Abnormal lipid profile includes the following either singly or in combination, triglyceride (TG) levels >150 mg/dl, high density lipoprotein cholesterol (HDL-C) (for men < 40 mg/dl and women > 50 mg/dl), low density lipoprotein cholesterol (LDL-C) >100mg/dl.

Lipid profile using RANDOX autoanalyser. All parameters expressed in milligram/decilitre. Cut-off values according to NCEP ATP III guidelines.<sup>7</sup>

### 3.6. Ncep atp iii criteria for lipids

**Table 1:** Cholesterol (mg/dL)

Cholesterol (mg/dL)	Category
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
>190	Very high

**Table 2:** Total Cholesterol (mg/dL)

Total Cholesterol (mg/dL)	Category
<200	Desirable
200-239	Borderline high
>240	High

**Table 3:** HDL Cholesterol (mg/dL)

HDL Cholesterol (mg/dL)	Category
<40	Low
>60	High

Also considered abnormal is an elevated total serum cholesterol level >200mg/dl

## 4. Sample Size estimation calculation

### 4.1. Sample size

This is a descriptive cross-sectional study which was done in the Department of Medicine, RRMCH, Bangalore.

50 cases of type 2 diabetes mellitus with abnormal fasting lipid profile (one or more lipid parameter) and 50

controls of type 2 diabetes mellitus with normal fasting lipid profile.

## 5. Data and Statistical Analysis

The data collected was analyzed using mean, mode for demographic data and frequency percentage for the analysis of the clinical data.

Statistical Analysis was done using SPSS software version 23.0. A 'p' value less than 0.05(p<0.05) is considered significant.

The various measures of central tendencies and graphical representations were used to analyze the data.

The data was analyzed using SPSS version 20. Mean and standard deviation will be applied between two groups. 't' test was applied to know the mean difference between two groups.

## 6. Observation and Results

### Descriptive statistics

**Table 4:** Age distribution among patients in the study

Age (years)	Number			Percentage		
	Cases	Controls	Total	Cases	Controls	Total
35-45	11	12	23			
Yeara				22.00%	24.00%	23.00%
46-55	17	21	38			
Years				34.00%	44.00%	38.00%
56-65	22	17	39			
Years				44.00%	34.00%	39.00%
Total	50	50	100	100.00%	100.00%	100.00%
				%	%	%

In the present study, when we evaluated the age distribution of the cases in the study we found that the most common age group was between the ages of 56-65 years, 39 patients belonged to this group with 22 patients in the test and 17 patients in the controls. 38 patients belonged to 46-55 years age group with 17 patients in the test and 21 patients in the controls. 23 patients belonged to 35-46 years age group with 11 patients in the test and 12 patients in the control respectively.

**Table 5:** Distribution of gender among patients in the

Gender	Number			Percentage		
	Cases	Controls	Total	Cases	Controls	Total
Male	30	31	61	60.00%	62.00%	61.00%
Female	20	19	39	40.00%	38.00%	39.00%
Total	50	50	100	100.00%	100.00%	100.00%

In the present study, 61.00% were males and 39.00% were females.

## 7. Discussion

Cardiovascular disease (CVD) is a significant cause of illness, disability, and death among individuals with

**Table 6:** Distribution based on regularity of treatment

Regularity of treatment	Cases	Number		Percentage		
		Controls	Total	Cases	Controls	Total
No treatment	0	0	0	0.00%	0.00%	0.00%
Irregular treatment	5	2	17	30.00%	4.00%	17.00%
Regular treatment	35	48	83	70.00%	96.00%	83.00%
Total				100.0	100.00	100.00

Most of the patients were on regular treatment (83 out of 100 patients). 35 patients (70.00%) and 48 patients (96.00%) of cases and controls respectively were on regular treatment. 15 patients in cases and 2 patients in controls were on irregular treatment.

**Table 7:** Comparison of mean fasting lipid parameters

Group	N	Minimum	Maximum	Mean	Std.deviation
<b>Cases</b>					
Ldl	50	196	299	229.70	19.810
Hdl	50	20	68	30.12	7.553
Tg	50	97	410	218.10	66.565
Total cholesterol	50	218	326	259.82	19.888
<b>Control</b>					
Ldl	50	79	137	110.16	13.365
Hdl	50	27	67	47.74	9.705
Total cholesterol-pp	50	150	229	192.50	17.210
TG-pp	50	92	263	183.20	40.069
Post prandial		Ldl	Hdl	Tg	Total
P Value		<0.001	<0.001	<0.001	<0.001

There is a statistically significant increase in total cholesterol, LDL and Triglycerides Value <0.05 in Fasting state of the cases compared to controls

**Table 8:** Comparison of mean postprandial lipid parameters

Group	N	Minimum	Maximum	Mean	Std.deviation
<b>Cases</b>					
Ldl-pp	50	216	319	259.50	19.431
Hdl-pp	50	17	65	27.12	7.553
Total cholesterol-pp	50	245	343	286.62	19.727
<b>Controls</b>					
Ldl-pp	50	110	168	141.76	13.540
Hdl-pp	50	30	70	50.74	9.705
Total cholesterol	50	150	229	192.50	17.210
Tg-pp	50	92	263	183.20	40.069
Post prandial		Ldl	Hdl	Tg	Total
P value		<0.001	<0.001	<0.001	<0.001

There is a statistically significant increase in total cholesterol, LDL and triglycerides (P value <0.05) in Postprandial state of the cases compared to controls.

**Table 9:** Comparison of mean lipid parameters within cases there is a statistically significant increase in total cholesterol, LDL, Triglycerides (P

Fasting	Minimum	Maximum	Mean	Std.deviation
LDL	196	299	229.7	19.81
HDL	20	68	30.12	7.533
TG	97	410	218.1	66.565
Total	218	326	259.82	19.888
<b>Postprandial</b>				
Minimum	Maximum	Mean	Std.deviation	
LDL-pp	216	319	256.5	19.431
HDL-pp	17	65	27.12	7.553
TG-pp	115	428	236.1	66.565
Total	245	343	286.62	19.727
	LDL	HDL	TG	Total
P value	<0.01	<0.05	<0.01	<0.01

value <0.05) in Postprandial state of the cases compared to their fasting state.

**Table 10:** Comparison of mean lipid parameters within controls There is a statistically significant increase in total cholesterol, LDL, Triglycerides, (Pvalue <0.05) in Postprandial state of the controls compared to their fasting state.

Fasting	Minimum	Maximum	Mean	Std.deviation
Ldl	79	137	110.16	21.816
Hdl	27	67	47.74	10.361
Tg	74	245	165.20	40.069
Total	127	194	157.90	21.833
<b>Postprandial</b>				
Minimum	Maximum	Mean	Std.deviation	
Ldl-pp	110	168	141.76	12.915
Hdl-pp	30.	70	50.74	9.697
Tg-pp	92	263	183	39.445
Total	150	229	192	16.80
	LDL	HDL	TG	Total
P value	<0.01	>0.05	<0.01	<0.01

**Table 11:** Comparison of fbs and ppbs within controls

	Cases	Controls	P value
Fbs	142.09	122.17	0.00
	+45.86	+33.42	
PPBS	212.35	181.96	0.00
	+67.97	+33.77	
P value	0.00	0.00	

There was a statistically significant increase in PPBS value in both cases and controls compared to their FBS values and also there is a significant increase in PPBS values in cases compared to PPBS values in controls (p = 0.00).

**Table 12:** Comparison of hba1c among cases and controls

Group	N	Minimum	Maximum	Mean	Std.deviation
Cases	50	5.7	8.4	7.142	0.8318
HBA1c					
Controls	50	4.6	6.2	5.554	0.367
HBA1C					

diabetes. The macrovascular complications of diabetes—Coronary Heart Disease (CHD), Cerebrovascular Accidents (CVA), and Peripheral Vascular Disease (PVD)—all being different facets of the same vascular damage – account for more than 70% of all deaths in individuals with diabetes.

CVD events are four times more common in individuals with diabetes, occur at a younger age, and have a much higher case fatality rate, this is more so in Indians. Coronary Artery Disease in Indians (CADI) is a phenomenon by itself. In fact, people with diabetes and no history of vascular disease have the same risk of having a heart attack or dying of vascular disease as non-diabetic individuals with a prior history of cardiovascular disease. Lipid and lipoprotein abnormalities are common in the diabetic population due to the effects of insulin deficiency and insulin resistance on key metabolic enzymes.

In our study the maximum number of patients had a duration of diabetes for >10 years. 30 patients had a duration of diabetes between 1-5 years. 39 and 30 patients had diabetes duration between 10 -15 years and >15 years respectively. In this study, distribution of fasting dyslipidemia (cases) is more in 56-65 yrs age group, while in study carried out Kusum Bali, et al the distribution of dyslipidemia among the different age groups was almost similar: 82.6% in < 45 years, 82.9% in 45-60 years and 83.7% in > 60 years, the difference was not statistically significant.<sup>61</sup> In our study we found the distribution of fasting dyslipidemia is slightly higher in males as compared to females, findings are consistent with the study by Kusum Bali, et al, where they found dyslipidemia is more in males (133 males out of 285 DM type 2 patients).

In the present study, we found fasting dyslipidemia was maximum in both cases and controls with the duration of diabetes >10 yrs. In the present study IHD was found in 14 out of 100 patients, 11 in cases and 3 in controls i.e. 22% and 6% respectively. Evidence of IHD was found more in cases compared to controls, statistical significance was found ( $p < 0.05$ ).

In a study carried out by R.P. Agrawal, et al in 4067 patients of DM 2 they found that the prevalence of CHD was 12.4% and the risk of CHD in known Type 2 diabetic patients was higher in men than in women. Of the diabetic men 60% showed high (20–40%) or very high (>40%) risk of CHD, while 56% of the women had values compatible with moderate (10–20%), mild (5–10%) or low (<5%) risk of CHD ( $p < 0.05$ ).

In a study carried out by Nafisa C Vaz, et al to determine the prevalence of diabetes mellitus (DM) and its associated diabetic complications in rural Goa, India, they found that among 1,266 study participants about 130 (10.3%) were diabetics. The prevalence of CHD (32.3%) was higher among the diabetics compared to non-diabetics (3.3%).<sup>65</sup> In the study carried out by Deepa D. V., et al in 100 newly diagnosed type 2 DM patients they found prevalence of

CAD as 26 % and ECG findings were normal in 74 cases, myocardial infarction (MI), left bundle branch block, left ventricular hypertrophy (LVH) in three cases each, old MI in seven cases, ischemic heart disease in six cases and arrhythmias in two cases. 2D- echocardiography showed regional wall motion abnormality in 23 cases, hypertensive heart disease in eight cases, concentric LVH and ischemic dilated cardiomyopathy in one case each

In study carried out by Pekka Koskinen, et al they found compared with nondiabetic subjects, non insulin-dependent diabetic patients (NIDDM) had higher triglyceride concentration ( $P < 0.0001$ ), lower HDL cholesterol ( $P < 0.001$ ), and greater BMI ( $P < 0.001$ ), there were more hypertensive patients among them ( $P < 0.001$ ). The incidence of myocardial infarction and cardiac deaths were significantly higher among diabetic than nondiabetic participants (7.4 vs. 3.3%, respectively) ( $P < 0.02$ )

In the present study, PVD was found in 25 out of 100 patients, 20 patients out of 50 in cases i.e. 40% and in controls it was found in 5 out of 50 patients i.e. 10%. Evidence of PVD was found more in cases as compared to controls with statistical significance ( $p < 0.05$ ).

In study carried out by Hiren P Pandya, et al they concluded On analysis of ABI among patients with diabetes mellitus, out of 50 patients, 9 (18%) were found not to have PAD (ABI < 1) and their lipid profile was within normal range, whereas 41 (82%) were found to have ABI of >1, and on comparative analysis of lipid profile, their TC, triglyceride, and LDL were significantly higher than those of patients having ABI of <1 ( $P < 0.05$ ). In a study carried out by Samson Okello, et al they found the prevalence of PAD (ABI of <0.9) was 24%. Among the patients with PAD, 87% had mild PAD (ABI 0.71-0.90) while 13% had moderate to severe PAD (ABI <0.70).

In a study carried out by Nafisa C Vaz, et al To determine the prevalence of diabetes mellitus (DM) and its associated diabetic complications in rural Goa, India they found Among the total 1,266 study participants about 130 (10.3%) were diabetics And prevalence of cerebrovascular accidents (CVAs) was 6.9%.

Carlo Bruno Giorda et al in a study prospectively followed-up 14 432 type 2 DM patients, aged 40 to 97 years. During a 4-year follow-up, they found 296 incident stroke events were recorded. In subjects with no history of cardiovascular disease, the age-standardized incidence of stroke was 5.5 in men and 6.3 in women (per 1000 person-years). In subjects with a history of cardiovascular disease, it was 13.7 in men and 10.8 in women. The ratios of incidence of stroke varied according to the age, sex, and history of cardiovascular disease. Among men with no history of CVD, HbA1c and smoking were the predictors of stroke. Among subjects with history, the risk factors in men were, therapy with oral agents plus insulin, treated high total cholesterol and a low HDL cholesterol, whereas in

women microvascular complications were a risk factor. The previous history of CVA was a strong predictor of stroke in both sexes.

In a study carried out by Seppo Lehto, et al they concluded that the risk of stroke in non-insulin dependent diabetes mellitus (NIDDM) men was about threefold and in NIDDM women fivefold higher than that in corresponding nondiabetic individuals. Low levels of HDL cholesterol (<0.90 mmol/L), high levels of total TGs (>2.30 mmol/L), and the presence of hypertension (HTN) were associated with a twofold increase in the risk of stroke mortality or morbidity.

In a study carried out by Jasmina Djelilovic-Vranic, et al Ischemic stroke was confirmed in 78.0%, of which 32% were lacunar infarcts and 22% hemorrhagic. The most common risk factors were hypertension 85%, then smoking in 65%, diabetes mellitus in 39.0%, in 27.38% dyslipidemia, the previous stroke in 26.69%, in 23.57% arrhythmia. In the baseline sample, 30.06% of patients had previously diabetes mellitus and in 8.94% the diabetes was diagnosed during hospitalization, while dyslipidemia was known from earlier in 22.0% and in 5.38% cases was detected during the hospitalization.

## 8. Summary

This study was conducted in the department of medicine, Rajarajeswari medical college and hospital Bangalore. In the present study 100 type 2 diabetic patients, divided into 50 cases and 50 controls satisfying inclusion criteria were considered.

The findings are summarized as follows:-

1. There was a significant elevation of mean values of total serum cholesterol, LDL and TG of cases and controls in the postprandial state compared to their fasting state, statistical significance was found ( $P < 0.05$ ).
2. Mean values of total serum cholesterol, LDL and TG of cases in fasting state were significantly more compared to controls in fasting state, statistical significance was found ( $P < 0.05$ ).
3. Mean values of total serum cholesterol, LDL and TG of cases in the postprandial state were significantly more compared to controls in the postprandial state, statistical significance was found ( $P < 0.05$ ).
4. Mean values of both FBS and PPBS in cases were higher compared to controls ( $P < 0.05$ ). Mean values of PPBS in cases and controls were significantly more compared to their respective FBS values ( $P < 0.05$ ).
5. The mean HbA1c values in cases were higher (7.142) compared to controls (5.554)

## 9. Conclusion

1. Prevalence of diabetes was highest in the age group 56-65 years in our hospital

2. As the duration of diabetes increases, there is an increased prevalence of dyslipidemia in the cases.
3. Past history of HTN, IHD, PVD and CVA were found significantly more in subjects with fasting and postprandial dyslipidemia (cases) compared to those without (controls).
4. Patients on irregular treatment (63%) were more in the study group (cases) compared to controls. So it could be said that patient not on regular treatment are more prone to have dyslipidemia. (fasting as well as postprandial).
5. There was a significant increase in total serum cholesterol, LDL and TG in postprandial states of cases compared to that in controls, so it could be said that diabetic patients with fasting dyslipidemia are more prone to have dyslipidemia in the postprandial state.
6. Cases were having significantly higher FBS and PPBS compared to the controls, so it could be said that as blood sugar increases the occurrence of dyslipidemia increases.
7. HbA1c was significantly higher in cases compared to controls, so it could be said that as HbA1c increases there is an increase in the occurrence of dyslipidemia.

## 10. Source of funding

None.

## 11. Conflict of Interest

None.

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