

Age Related Dyslipidemia in Type 2 Diabetes Mellitus Patients: A Hospital Based Prospective Study

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Abstract:

Objectives: The present study was to evaluate the lipid profile and to establish the relation between serum lipid profile of type 2 Diabetes mellitus patients in different age group and it was also evaluate the effect of duration of diabetes mellitus on lipid profile.

Methods: A total of 80 subjects were enrolled in this study. The patients were divided into two major groups, one group comprising 40 patients in old age group (DDO) with diabetes and dyslipidemia were included and second group 40 comprised of old age non-diabetic but dyslipidemic patients (NDDO). The diagnosis of diabetes mellitus was based on World Health Organization (WHO) criteria. All the biochemical estimations were done by using RFCL kit on the micro lab -300 Semi Auto- analyser.

Results: FBS and PPBS were significantly higher in DDO group as compared to NDDO group ($p < 0.0001$). Mean TC level of DDO and NDDO group was 319.645 ± 38.765 and 335.332 ± 42.887 respectively, but it was not statistically significant ($p = 0.0901$). Mean HDL of DDO and NDDO group was 30.732 ± 3.612 and 34.675 ± 4.321 respectively and it was statistically significant differences ($p < 0.0001$). Mean LDL of DDO and NDDO group was 218.657 ± 38.241 and 226.689 ± 43.223 , but it was not statistically significant ($p = 0.3814$). Mean VLDL of DDO and NDDO group was 80.342 ± 5.123 and 72.881 ± 7.665 respectively, and it was statistically significant differences ($p < 0.0001$). Mean TG of DDO and NDDO group was 361.721 ± 39.476 and 363.788 ± 31.445 respectively, but it was not statistically significant ($p = 0.7963$).

Conclusions: disturbances of lipid profile are more common in old age diabetic patients. Increasing age and diabetic state, both are the most common factors which affect the lipid profile.

Keywords: Type 2 diabetes mellitus, Dyslipidemia, old age.

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Introduction

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or most commonly both. The worldwide prevalence of diabetes mellitus (DM) has risen dramatically over past two decades from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, more than 360 million individuals will have diabetes by the year 2030[1].

Type 2 diabetes is a global public health problem that is known to be associated with increased cardiovascular mortality and morbidity. People with diabetes have a 2 to 4-fold increase in the risk of ischemic heart disease, a 2- fold increase in stroke risk and a 4 to 8 years reduction in life expectancy [2,3]. Dyslipidemia, characterized by an abnormal lipid profile, is one of the major risk factors for cardiovascular disease in patients with diabetes [4], and is mainly due to increased free fatty acids flux

secondary to insulin resistance [5]. Metabolic syndrome with its associated insulin resistance leads to increased lipolysis by reducing inhibition of hormone-sensitive lipase in adipose tissue, thereby stimulating portal flux of free fatty acids to the liver [6,7]. These fatty acids in turn disrupt the activity of the hormone lipoprotein lipase causing an overproduction of triglyceride-rich lipoproteins [very-low-density lipoprotein (VLDL) and Chylomicrons] which are commonly associated with a reduction in HDL-c and an increase in small dense oxidized LDL-c levels [8,9]. The prevalence of dyslipidemia among patients with type 2 DM is high [10]. In a study conducted in Yemen, the prevalence of diabetic dyslipidemia among patients with type 2 DM was 85% and the common patterns of dyslipidemia in that study were high LDL-C followed by high serum cholesterol level [11].

Top of Form

After the age of 20 years, the LDL cholesterol concentration increases progressively in men and women, but more rapidly in men, accounting for most of the overall gender difference in total cholesterol.

The LDL cholesterol levels reach a plateau in men between the age of 50 and 60 years, and in women between the age of 60 and 70 years [12]. Serum high-density lipoprotein (HDL) cholesterol levels decrease in male during puberty and early adulthood, and thereafter remain lower than in women at all comparable ages. On the other hand, the HDL cholesterol concentrations remain constant in women throughout their lifetime [13]. The triglyceride concentrations increase progressively in men, reaching peak values between 40 and 50 years of age, and decline slightly thereafter. In women, the triglyceride concentrations increase throughout their lifetime, and are always higher in those using estrogens [13].

Essentially before menopause, women usually have total cholesterol levels that are lower than those of men of the same age. As women and men get older, their blood cholesterol levels rise until about 60–65 years of age. In women, menopause often causes an increase in their LDL cholesterol and a decrease in their HDL cholesterol level, and after the age of 50, women often have higher total cholesterol levels than men of the same age. This may well be one factor as to why the incidence of atherosclerotic disease rises dramatically in postmenopausal women [13]. A mechanism that could explain the age-related changes in lipid metabolism is pseudo-capillarization of the liver sinusoidal endothelial cells dysfunction. This physiologic phenomenon has been described in elderly humans and some animals. It leads to decreased endocytosis, increased leukocytes adhesion, decreased hepatic perfusion, and potentially affects passage of chylomicron remnants to hepatocytes [14].

Distribution of abnormal lipid profile amongst the different cadre of age groups, middle aged, elderly and the young made up 247 (42%), 317 (52%) and 36 (6%) respectively of the study population. Triglyceride was the only lipid parameter that differed significantly in the three age groups. Elevated triglyceride was more significantly elevated in the middle and elderly age group than in the younger age group.

The prevalent combination of lipid abnormalities was that of elevated TG and reduced HDL, two defining parameters of the metabolic syndrome. These two lipid abnormalities are the most commonly noted abnormalities of the standard lipid profile in subjects with obesity and insulin-resistance-related cardio metabolic risk Total cholesterol level gradually increases with age. After

the age of about 55 years, women consistently have higher total LDL and HDL cholesterol level than do men of the same age. The value of total cholesterol as predictor of the relative risk of coronary disease with increasing age in both men and women. In the Framingham study, Cholesterol levels over 275 mg/dl (7.1 mmol/L) were associated with a fourfold increase in risk of recurrent infarction or in coronary death, and almost a threefold increase in risk from all-cause mortality compared with Cholesterol levels less than 200 mg/ dl [15]. Lipoproteins are altered in diabetes.

The quantitative changes, most commonly seen are an increase in the TG-rich lipoproteins and a decrease in HDL [14,16]. These changes can be seen at and even before the diagnosis of diabetes. Serum high-density lipoprotein (HDL) levels decrease in males during puberty and early adulthood, and thereafter remain lower than in women at all comparable ages. On the other hand, the HDL-c concentrations remain constant in women throughout their lifetime [15]. Triglyceride concentration increases progressively in men, reaching peak values between 40 and 50 years of age, and declines slightly thereafter. In women, the triglyceride concentration increases throughout their lifetime, and are always higher in those using estrogens.

Objectives of our study were to evaluate the lipid profile and to establish the relation between serums lipid profile of type 2 Diabetes mellitus patients in different age group. And it was also evaluate the effect of duration of diabetes mellitus on lipid profile.

Materials and Methods

The present study was conducted in the Department of Biochemistry in AIIMS, Patna during a period from January 2022 to December 2022. The patients were in uniformity in socioeconomic status, culture and food habits.

A total of 80 subjects were enrolled in this study. The patients were divided into two major groups, one group comprising 40 patients in old age group (DDO) with diabetes and dyslipidemia were included and second group 40 comprised of old age non-diabetic but dyslipidemic patients (NDDO).

Inclusion criteria

The participants were allowed to pursue their treatment schedules and regular lifestyles during this study including drug intake & tobacco addiction. (Smokers were defined as consuming ≥ 5 cigarettes per day and were smoking continuously for a minimum of six months prior to being enrolled.

Informed consent was obtained from all individuals for participating in the study.

Exclusion criteria

Patients less than or equal to ≥ 25 years of age were excluded from the study.

Subjects suffering from any other hormonal disorders, benign or malignant disorders, diabetic ketoacidosis, febrile conditions, renal failure and other renal diseases, gastroenterological conditions, liver diseases, transplant rejection, diseases of the central nervous system and pregnant ladies were excluded from the study.

Study Design

Randomly selected diabetic patients were subjected to evaluation for lipid profile, clinically and biochemically. The diagnosis of diabetes mellitus was based on World Health Organization (WHO) criteria i.e. Fasting plasma glucose of 126 mg/dl (7.0 mmole/L) or more, after a minimum of 12-hour fasting, with symptoms of diabetes.

A 2 hours - post prandial plasma glucose level of equal or more than 200 mg/dl (11.1mmole/L).

Procedures: Old diabetics were also re-confirmed for their present biochemical status. Post prandial blood samples were drawn 2 hours after ingestion of glucose in 300 ml of water (@ 1.75 grams of glucose per kg body weight with a maximum of 75 gms of glucose). Fasting blood samples were used for estimation of all the parameters except for the postprandial serum glucose estimation. All the biochemical estimations were done by using RFCL kit on the microlab -300 Semi Auto- analyzer. Fasting and postprandial serum glucose was estimated quantitatively by GOD/POD technique as described by Trinder (1969). Total cholesterol was

estimated quantitatively by CHOD-PAP technique as described by Allian C.C (1974). Serum Triacylglycerol was estimated quantitatively by GPO-ESPAS technique as described by Buccolo G and David M (1973). High density lipoproteins (HDL-C) were estimated quantitatively by PEG-PAP method.

Very low density lipoproteins (VLDL-C) were estimated from serum triacylglycerol level using Friedewald formula. Low density lipoproteins (LDL-C) was calculated by subtracting serum HDL and VLDL from total serum cholesterol. Patients suffering from both the conditions included in the study underwent other relevant investigations at their first visit and on follow-up.

Ethical clearance was taken from the institution prior to the commencement of the study. All the observed data regarding patients were documented as prescribed Performa.

Statistical Analysis

Data analysis and calculation of statistical parameters were done by using SPSS and Microsoft excel software. Two tailed Student's t test was used compare the means of different parameters. P values was taken less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

Results

A total 80 subjects were included in this study. Out of 80 cases, 40 old age (50-60 years) patients of type 2 diabetes mellitus with dyslipidemia were enrolled in case group I and 40 old age (>60 years) patients of non-diabetic with dyslipidemia were enrolled in case group II.

Table 1: Demographic details of case and control

Groups		Numbers (n)	Mean Age(Yrs) \pm SD
Case group	DDO	40	59.89 \pm 0.487
	NDDO	40	68.95 \pm 0.789

As shown in table 1, mean age of case group of DDO was 59.89 \pm 0.487 years. While, mean age of NDDO groups was 68.95 \pm 0.789 years.

Table 2: Blood sugar levels and lipid profiles in old aged Diabetic and Dyslipidemic Patients (DDO) (n=40)

	Mean (mg/dl)	SD
FBS	180.342	33.234
PPBS	257.231	45.564
TC	319.645	38.765
HDL	30.732	3.612
LDL	218.657	38.241
VLDL	80.342	5.123
TG	361.721	39.476

As shown in table 2, FBS and PPBS levels were 180.342 \pm 33.234 mg/dl and 257.231 \pm 45.564 mg/dl respectively in DDO group. Mean TC, HDL, LDL, VLDL, and triglyceride level were 319.645 \pm 38.765 mg/dl, 30.732 \pm 3.612 mg/dl, 218.657 \pm 38.241 mg/dl, 80.342 \pm 5.123 mg/dl and 361.721 \pm 39.476 mg/dl respectively.

Table 3: Blood sugar levels and lipid profiles in DDO group with history of DM < 5 Yrs. (n=20)

	Mean (mg/dl)	SD
FBS	168.564	29.987
PPBS	221.165	30.765
TC	308.743	37.879
HDL	31.564	3.655
LDL	212.996	38.731
VLDL	81.098	6.221
TG	339.877	33.554

Table 4: Blood sugar levels and lipid profiles in DDO group with history of DM > 5 Yrs. (n=20)

	Mean (mg/dl)	SD
FBS	194.876	31.879
PPBS	277.322	42.786
TC	326.566	37.988
HDL	30.788	2.001
LDL	223.112	38.976
VLDL	82.654	1.001
TG	386.878	29.453

In table 3 and 4 we compared lipid profiles of DDO group with history of diabetes < 5 yrs and > 5 yrs. Mean total cholesterol LDL, VLDL and TG were significantly higher in DDO with history of DM > 5 yrs. HDL level was significantly lower in later group.

Table 5: Blood sugar levels and lipid profiles in non-Diabetic Dyslipidemic (NDDO) Patients (n=40)

	Mean (mg/dl)	SD
FBS	94.443	13.554
PPBS	134.655	16.778
TC	335.332	42.887
HDL	34.675	4.321
LDL	226.689	43.223
VLDL	72.881	7.665
TG	363.788	31.445

As shown in table 5, mean FBS and PPBS levels were 94.443 ± 13.554 mg/dl and 134.655 ± 16.778 mg/dl respectively in NDDO group. Mean TC, HDL, LDL, VLDL and triglyceride level were 335.332 ± 42.887 mg/dl, 34.675 ± 4.321 mg/dl, 226.689 ± 43.223 mg/dl, 72.881 ± 7.665 mg/dl and 363.788 ± 31.445 mg/dl respectively.

Table 6: Comparison of DDO group with NDDO group patients.

		Mean (mg/dl)	SD	P Values
FBS	DDO	180.342	33.234	<0.0001
	NDDO	94.443	13.554	
PPBS	DDO	257.231	45.564	<0.0001
	NDDO	134.655	16.778	
TC	DDO	319.645	38.765	0.0901
	NDDO	335.332	42.887	
HDL	DDO	30.732	3.612	<0.0001
	NDDO	34.675	4.321	
LDL	DDO	218.657	38.241	0.3814
	NDDO	226.689	43.223	
VLDL	DDO	80.342	5.123	<0.0001
	NDDO	72.881	7.665	
TG	DDO	361.721	39.476	0.7963
	NDDO	363.788	31.445	

As shown in table 6, FBS and PPBS were significantly higher in DDO group as compared to NDDO group ($p < 0.0001$). Mean TC level of DDO and NDDO group was 319.645 ± 38.765 and 335.332 ± 42.887 respectively, but it was not statistically significant ($p = 0.0901$). Mean HDL of

DDO and NDDO group was 30.732 ± 3.612 and 34.675 ± 4.321 respectively and it was statistically significant ($p < 0.0001$). Mean LDL of DDO and NDDO group was 218.657 ± 38.241 and 226.689 ± 43.223 , but it was not statistically significant ($p = 0.3814$). Mean VLDL of DDO and

NDDO group was 80.342 ± 5.123 and 72.881 ± 7.665 respectively, and it was statistically significant ($p < 0.0001$). Mean TG of DDO and NDDO group was 361.721 ± 39.476 and 363.788 ± 31.445 respectively, but it was not statistically significant ($p = 0.7963$).

Discussions

Diabetes mellitus is an endocrine disorder which is characterized by metabolic abnormalities with micro and macrovascular complications which cause significant morbidity and mortality [17,18]. India is one of the rapidly developing country standing in second highest diabetes prevalence in the world which could be due to rapid urbanization that brought along with it a sedentary lifestyle is an important factor inducing diabetes mellitus [17,19].

Various factors are known to affect the lipid profile like age, sex, BMI, diabetic state etc. Dyslipidemia has various deleterious effects on health like increased incidence of atherosclerosis and myocardial infarction. When associated with diabetes mellitus effects of dyslipidemia worsen many times. As there are limited studies available on age related change in lipid profile in diabetic subjects, this study was conducted to find out correlation of age with dyslipidemias. This cross-sectional case study was carried out on total of 80 cases. Out of 80 cases, The patients were divided into two groups, one group case I comprising 40 patients in old age group (50-60) (DDO) with diabetes and Dyslipidemia and second group (n=40) case II comprised of old age non-diabetic but dyslipidemic patients (NDDO).

Table 1 shows demographic details of all cases. Mean age of DDO and NDDO groups were 59.89 ± 0.487 years. And 68.95 ± 0.789 years respectively. While sex ratio in in these three groups were 4.12 and 1.87 respectively. Higher incidence of diabetes mellitus in males is consistent with the findings of many authors who stat that there is increased prevalence of diabetes in males specially in older age groups [20].

As shown in table 2, in DDO group lipid profile was similarly associated with age as in DDM group. There is a positive correlation between age and TC, LDL, VLDL and triglyceride. HDL was negatively correlated with age. These findings can again be explained by the studies of Miller et al. [21] and Framingham et al. [22].

Our findings were also supported by the study of Walter et al. [23] Who has found that the blood-lipid profile worsened with increasing age. Specifically, triglycerides, total cholesterol, and LDL cholesterol increased within each age-group (31, 16, and 15%, respectively). No consistent effect of age was noted on HDL cholesterol and the total cholesterol-to-HDL cholesterol ratio.

In table 3 and 4 we compared lipid profiles of DDO group with history of diabetes < 5 yrs and > 5 yrs. Mean total cholesterol LDL, VLDL and TG were significantly higher in DDO with history of DM > 5 yrs. HDL level was significantly lower in later group.

As shown in table 5, in NDDO group mean FBS and PPBS levels were well within normal range, they were 94.443 ± 13.554 mg/dl and 134.655 ± 16.778 mg/dl respectively.

When we compared DDO with NDDO group to find out the effects of DM over lipid profiles (table 6). FBS and PPBS were significant higher in DDO group as compared to NDDO group. Mean TC, HDL, LDL, VLDL and triglyceride level were 335.332 ± 42.887 mg/dl, 34.675 ± 4.321 mg/dl, 226.689 ± 43.223 mg/dl, 72.881 ± 7.665 mg/dl and 363.788 ± 31.445 mg/dl respectively in NDDO group. While in DDO group mean TC, HDL, LDL, VLDL and triglyceride level were 319.645 ± 38.765 mg/dl, 30.732 ± 3.612 mg/dl, 218.657 ± 38.241 mg/dl, 80.342 ± 5.123 mg/dl and 361.721 ± 39.476 mg/dl respectively. In NDDO group TC, LDL, and Triglyceride levels were higher but not statistically significant while VLDL levels were significantly lower as compared to DDO. Age and diabetic state both are known to affect the lipid profiles. Above picture of lipid profile can be explained by presence of one factor in each group. Effects of old age (> 60 yrs.) on lipid profile (except VLDL) in NDDO might have been antagonized by the effects of DM on lipid profiles.

Above result analysis was established a significant correlation of lipid profile with aging in diabetic and nondiabetic individuals. Effects of age on lipid profile derangement were greater than diabetic state.

In a study by Singh G et al, found the incidence of dyslipidemia as 59% of type 2 diabetics had hypercholesterolemia, 53% had hypertriglyceridemia, 98% had abnormal LDL levels and 89% had the HDL less than 40 mg/dl [24]. In another study by Bali K et al, the incidence of dyslipidemia in type 2 diabetic patients of Punjab population was reported as 81.8% and hypercholesterolemia as 36.5%, hypertriglyceridemia as 57.2%, high LDL levels as 59.3% and low HDL as 34.4% patients where the hypertriglyceride incidence was high and reduced HDL incidence was very less [25].

Summary

Total cholesterol, LDL, VLDL and triglyceride levels were increased in old aged sub groups (DDO) of diabetic patients as compared to non-diabetic dyslipidemic NDDO patients group. HDL level was

decreased in diabetic with dyslipideic groups (DDO) as compared to non-diabetic with dyslipidemic (NDDO) patients group. Age as well as diabetic state both were affected factors of lipid profile.

In diabetic with dyslipidemic patient (DDO) lipid profile was more severely affected as compared with non-diabetic with dyslipidemic patients group. Age had stronger effects on lipid profile than the effects of diabetic state which was evident during comparison of diabetic patients with older (more than 60 years) non-diabetic subjects. Duration of diabetes mellitus had also a deleterious effect on lipid profile which was evident from the comparison of subjects having history of DM more than 5 years and less than 5 years.

Conclusion

The present study concluded that the disturbances of lipid profile are more common in old age diabetic patients. Increasing age and diabetic state, both are the most common factors which affect the lipid profile.

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