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A Cross-sectional Study on Age related Dyslipidaemia in patients with Type-2 Diabetes mellitus

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Abstract
Objectives: *This study was to evaluate the effect of duration of diabetes mellitus on lipid profile of different age groups patients, establish the relation between serums lipid profile of patients with type 2 Diabetes mellitus with aging.*
Methods: *A detail history, clinical examination and relevant investigations were performed all patients. Plasma glucose estimation was performed by using RFCL kit on the microlab -300 Semi Auto- analyzer supplied by Merck. Total cholesterol was estimated quantitatively by CHOD-PAP technique. Serum Triacylglycerol was estimated quantitatively by GPO-ESPAS technique. High density lipoproteins (HDL-C) was estimated quantitatively by PEG-PAP method. Very low density lipoproteins (VLDL-C) was estimated from serum triacylglycerol level using Friedewald formula and low density lipoproteins (LDL-C) was calculated by subtracting serum HDL and VLDL from total serum cholesterol.*
Results: *Data was analyzed by SPSS software. Mean ± S.D and Person's r value were observed. P value was taken ≤ 0.05 for significant differences.*
Conclusions: *This study was concluded that age as well as diabetic state had deleterious effects on lipid profile. All constituent of lipid profile had an increasing trend with age except HDL which had a negative trend with advancing age; this was true in diabetic and non diabetic subjects as well. Hence, we may be suggested that diabetes mellitus accelerates age related disturbance in lipid profile.*
Keywords: *Age, Dyslipidemia, Type 2 diabetes mellitus, Plasma glucose, lipid profile.*

Introduction

Diabetes mellitus, long considered a disease of minor significance to world health, is now taking its place as one of the main threats to human health in the 21st century.[1]

The world population of older adults is increasing significantly. By the year 2050 adults older than 65 year will comprise one- fifth of the global population. In India there are now about 80 million individuals aged 60 years and older and by

2025 these will grow further to 168 million approx. Of Indian population interestingly the age group 85 and older is the fastest growing segment of the population and at present rate of growth there will be more than 3,80,000 centenarians by the year 2030.[2,3]

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.(4)

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.[5]

Objectives of this study were to evaluate the lipid profile in details in diabetic patients of different age groups, establish the relation between serums lipid profile of Diabetes mellitus type -2 and aging and found out the effect of duration of diabetes mellitus on lipid profile.

Materials and Methods

Study Subjects

A total 108 subjects were randomly selected with irrespective of sex into case group, out of which 72 patients were diabetes with dyslipidemic while 36 patients were non diabetic with dyslipidemic. Diabetic patients were divided in two age groups, 36 cases were of Diabetic Dyslipidemic Middle aged groups 40-50 years (DDM) and 36 were Diabetic Dyslipidemic Old aged groups 50-60 years (DDO). Another 36 cases were of Nondiabetic Dyslipidemic Old aged (NDDO), above 60 years. Control group was consisted of 36 healthy subjects.

Data was collected in the Department of Biochemistry, Katihar Medical College and Hospital in collaboration with the Department of Medicine during a period from December 2012 to October 2013. All subjects signed an inform consent approved by institutional ethical committee of Katihar Medical College, Katihar, Bihar, India was sought.

Inclusion criteria were the participants were allowed to pursue their treatment schedules and regular lifestyles during this study including drug intake & tobacco addiction.

Exclusion criteria: Patients less than or equal to ≥ 25 years of age, other hormonal disorders, benign or malignant disorders, diabetic ketoacidosis, febrile conditions, renal failure, other renal diseases, gastroenterological conditions, liver diseases, transplant rejection, diseases of the central nervous system and pregnant ladies were excluded from the study.

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).

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 grams 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 supplied by Merck. 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) was estimated quantitatively by PEG-PAP method. Very low density lipoproteins (VLDL-C) was 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.

Estimation of plasma Glucose

Method: Glucose oxidase peroxidise (GOD-POD) end point colorimetry (RFCLkit).

Principle: Glucose is oxidised to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4- amino antipyrine by the catalytic action of peroxidise to form a red colored quinonimine dye complex. intensity of the colour is directly proportional to the amount of glucose present in sample.

Statistical Analysis

Data was analyzed by using SPSS software. Mean ± S.D and Person's r value were observed. P value was taken equal to or less than 0.05 for significant differences.

Results

In this present study, mean age of overall case group was 56.51 ± 0.865 years while sex ratio was 1.57. Mean age of DDM, DDO and NDDO groups were 46.02 ± 0.422 years., 56.77 ± 0.392 years. and 66.75 ± 0.637years respectively. While the sex ratio in these three groups were 1.25, 3.50 and 1.00 respectively. Mean age of control group was 35.19 ± o.437 yrs. and sex ratio was 2.60.

Lipid profile and blood glucose level in Middle aged (40-50 years) Diabetic Dyslipidemic Patients (DDM) (n=36): mean FBS and PPBS levels were 202.6 mg/dl and 268.72 mg/dl respectively in DDM group. Mean TC, HDL, LDL, VLDL and triglyceride level were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 4.7, 0.31, 0.25 and 0.26 respectively. HDL is negatively correlated with age with r value -.41.

In this present study out of 36 cases of DDM, 18 cases had history of DM < 5 years, mean FBS and RBS levels were 185.50 ± 28.867mg/dl and 246.38 ± 47.95 mg /dl respectively in DDM < 5 years group. Mean TC, HDL, LDL, VLDL and triglyceride level were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 0.242, 0.228, 0.319 and 0.412 respectively. HDL is negatively correlated with age with r value -0.315.

Similarly, in this present study out of 36 cases of DDM, 18 cases had history of DM> 5 years, mean FBS and PPBS levels were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 0.234, 0.345, 0.305 and 0.305 respectively. HDL was negatively correlated with age with r value -0.42.

Comparison of Lipid profile and blood glucose level in subjects of DDM group with history of DM < 5 years and > 5 years. (n=18) was shown that significant higher values of PPBS and FBS in DDM with DM > 5 yrs as compared to DDM with DM < 5 yrs. Levels of all parameters of lipid profile except HDL were significantly higher (p < 0.05) in DDM with DM > 5 yrs as compared to DDM with DM < 5 yrs.

Blood sugar levels and lipid profiles in old aged Diabetic and Dyslipidemic Patients (DDO) (n=36): mean FBS and PPBS levels and mean TC, HDL, LDL, VLDL and triglyceride level were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 0.360, 0.175, 0.681 and 0.216 respectively. HDL was negatively correlated with age with r value –0.129

When we were compared lipid profiles of DDO group patients with history of diabetes < 5 years and > 5 years. 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.

Blood sugar levels and lipid profiles of non Diabetic Dyslipidemic (NDDO) Patients (n=36): Mean FBS and PPBS levels and TC, HDL, LDL, VLDL and triglyceride level were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 0.364, 0.451, 0.275 and 0.206. respectively. HDL was negatively correlated with age with r value -0.156.

When we were observed blood sugar level and lipid profile of cases of control group (n=36): mean FBS and PPBS levels and mean TC, HDL, LDL, VLDL, triglyceride level were a positive correlation between age and TC, LDL, VLDL and triglyceride with r values 0.116, 0.104, 0.142 and 0.142 respectively. HDL is negatively correlated with age with r value -0.049.

When we were compared the cases of DDM group with cases of control group, mean FBS, RBS levels and mean TC, HDL, LDL, VLDL and triglyceride level of DDM group and with control group. All these parameters were significantly higher in DDM group as compared to control group.

Comparison of DDO group with control: mean FBS and PPBS levels in DDO group were significantly higher than control group. Mean TC, HDL, LDL, VLDL and triglyceride level of DDO group and control group were significantly higher in DDO group.

Comparison of NDDO group with control: mean FBS and PPBS levels in NDDO group were within normal range. There was no significant difference in FBS or PPBS levels between NDDO and control group. Mean TC, HDL, LDL, VLDL and triglyceride level were significantly higher in NDDO group.

Comparison of DDM group with DDO: mean FBS and PPBS levels were significantly higher in DDM group as compared to DDO group. Mean TC, LDL, VLDL levels were significantly higher in DDO group as compared to DDM group while HDL levels were significantly lower in DDO group.

Comparison of DDM group with NDDO: FBS and PPBS were significant higher in DDM group as compared to NDDO group. While mean TC, HDL, LDL, VLDL and triglyceride levels were significantly higher in NDDO group.

Comparison of DDO group with NDDO: NDDO group TC, LDL, and Triglyceride levels were higher but not statistically significant while VLDL levels were significantly lower.

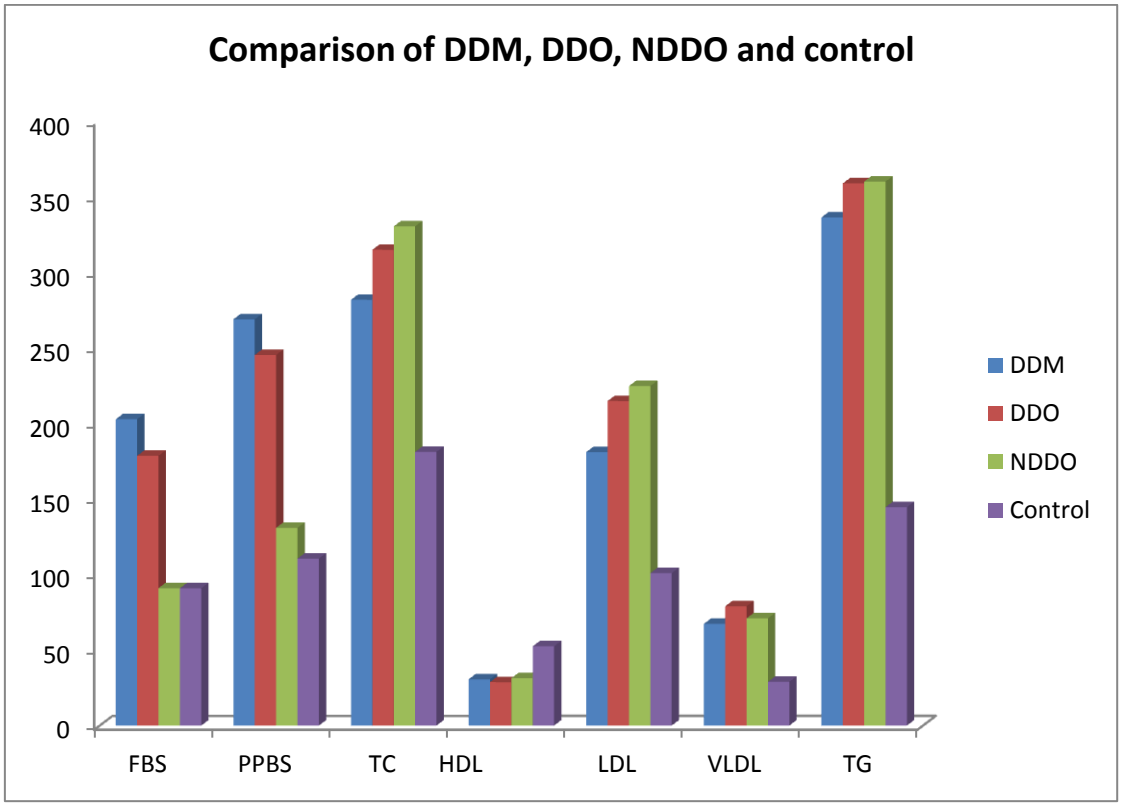
Table 1 Comparison of DDM, DDO, NDDO and control group

	Age	FBS	PPBS	TC	HDL	LDL	VLDL	TG
DDM	46.0 ±0.4	202.6 ±44.6	268.72 ±54.6	281.6 ±39.3	30.58 ±2.54	180.85 ±38.0	67.22 ±7.43	336.1 ±37.1
	R	.164	.023	.470	-.415	0.31	.254	.264
DDO	56.7± 0.3	178.4± 31.1	245.13 ±43.85	314.7 ±36.8	28.6 9±2.0	214.66 ±36.4	78.87 ±3.05	358.63 ±37.63
	r	-0.73	-0.728	0.360	-0.12	0.175	0.681	0.216
NDDO	66.7 ±0.63	90.8 ±12.3	130.8 ±12.8	330.2 ±40.5	31.3 ±2.48	224.58 ±39.52	70.93 ±6.21	359.83 ±28.34
	R	.408	.534	.364	-.156	.451	.275	.206
CONTROL	35.19 ± o.4	90.80± 11.69	110.4± 5.47	181.00 ±10	52.44 ±2.93	100.8 ±9.9	28.89 ±1.37	144.47 ±6.8
	r	.287	.143	.116	- .049	.104	.142	.142

As shown table no.1 Mean FBS level was highest (202.61±44.67mg/dl) in DDM group and lowest (90.80±11.69mg/dl) in control group. Similarly Highest (268.72 ±54.6mg/dl) PPBS level was found in DDM group while lowest value (110.44± 5.47mg/dl) was observed control group.

A highest level of total cholesterol (330.22 ±40.54 mg/dl) was found in NDDO group while lowest level was seen in controls. In all groups age was positively correlated with total cholesterol levels but strongest correlation was found in DDM group with persons r value 0.460.Mean HDL level was highest (52.44±2.93mg/dl) in control while lowest

(28.69±2.05mg/dl) in DDO group. HDL levels were negatively correlated with age in all age groups. Strongest association was observed in DDM with persons r value - 0.415.LDL level was highest (224.58±39.52 mg/dl) in NDDO group and lowest level (100.8±9.9 mg/dl) was observed in controls. In all age group there was a positive correlation between age and LDL levels. Strongest correlation was reviled in NDDO group with r value of 0.451. Triglyceride level was found maximum (359.83±28.34 mg/dl) in NDDO group and minimum in controls (144.47±6.8 mg/dl). As with other parameters TG was also positively correlated with age in all groups and the strongest correlation was seen in DDM group. A corresponding change was observed in levels of VLDL.



Graph 1 Comparison of blood sugar and lipid profile of cases with DDM, DDO, NDDO and Control

Discussion

Diabetes mellitus (DM) is a syndrome consisting of metabolic, vascular and neuropathic components that are interrelated. It is defined as group of metabolic disorder that is characterized by hyper-glycemia resulting from defect in insulin secretion, insulin action or both.

In this present study, Mean age of DDO and NDDO groups were 56.77 ± 0.392 yrs. and 66.75 ± 0.637 yrs. respectively. While sex ratio in these two groups were 3.50 and 1.00 respectively. In this present study, there were significant higher values of PPBS and FBS in DDM with DM > 5 yrs as compared to DDM with DM < 5 years. Levels of all parameters of lipid profile except HDL were significantly higher ($p < 0.05$) in DDM with DM > 5 yrs as compared to DDM with DM < 5 yrs. This signifies that changes in lipid profile are duration dependent. Derangement in lipid profile becomes worse with time.

In this present study, DDO group lipid profile was 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.[6] and Walter et al.[7]

In this present study, mean total cholesterol LDL, VLDL and TG were significantly higher in DDO with history of DM > 5 years. HDL level was significantly lower in later group.

In this present study, mean FBS and PPBS levels of cases with NDDO group were well within normal range. As in DDO group mean TC, LDL, VLDL and triglyceride level in NDDO were correlated with age. Mean FBS and PPBS levels in DDO group were significantly higher than control group. Mean LDL of group was significantly higher (p=0.003) than in control group There is rise in mean TC level secondary to rise in LDL level. Total cholesterol was significantly (p = 0.005) higher in DDO group as compared to control group. Mean HDL level of DDO group was significantly low (p = 0.001) as compared to control group. Mean triglyceride and VLDL was also significantly high in DDO group p values 0.002 and 0.01 respectively.

In this present study, there were no significant differences in FBS or PPBS levels between NDDO and control group. Mean TC, HDL, LDL, VLDL and triglyceride level of NDDO group and control group were compared. It was significantly higher in NDDO group. While HDL level was lower in NDDO group. (p=0.02).

Numerous studies by Taskinen MR (2003)[8] showed a similar dyslipidemic features among middle aged and old aged diabetic patients. In another Study, 13% of men and 24% of women with diabetes mellitus had increased total plasma cholesterol levels, compared with 14% of men and 21% of women without diabetes mellitus.[7]

In this present study, mean FBS (p=0.009) and PPBS (p=0.04) levels were significantly higher in DDM group as compared to DDO group. Mean TC, HDL, LDL, VLDL and triglyceride level of DDO group and mean TC, HDL, LDL, VLDL and triglyceride level of DDM group were significantly higher in DDO group as compared to DDM group while HDL (p= 0.0009) levels were significantly lower in DDO group. This comparison signified the influence of age over lipid profile in diabetic subjects.

When we were compared DDO with NDDO group to find out the effects of DM over lipid profiles. FBS and PPBS were significant higher in DDO group as compared to NDDO group. When Mean TC, HDL, LDL, VLDL and triglyceride level of NDDO group were compared with DDO group. It was found that 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.

We were compared the biochemical parameters of all groups cases. Mean FBS level was highest in DDM group and lowest in control group. Similarly the highest PPBS level was found in DDM group while lowest value was observed in control group. Highest levels of total cholesterol were found in NDDO group while lowest level was seen in control group. Mean HDL level was highest in control while the lowest was in DDO group. LDL level was highest (224.58±39.52 mg/dl) in NDDO group and lowest level (100.8±9.9 mg/dl) was observed in controls. Triglyceride level was found maximum (359.83±28.34 mg/dl) in NDDO group and minimum in controls (144.47±6.8 mg/dl). In all groups age was positively correlated with total cholesterol levels and the strongest correlation was found in DDM group with Person's r value 0.460. HDL levels were negatively correlated with age in all age groups. Strongest association was observed in DDM with Person's r value - 0.415. In all age groups there were a positive correlation between aging and LDL levels. Strongest correlation was reviled in NDDO group with r value of 0.451. As with other parameters TG was also positively correlated with aging in all groups and the strongest correlation was seen in DDM group. A corresponding change was observed in levels of VLDL.

Summary

1. All constituents of lipid profile were deranged in diabetic patients.
2. Total cholesterol, LDL, VLDL and triglyceride levels were increased in middle and old aged sub groups (DDM and DDO) of diabetic patients as compared to normal control subjects.
3. HDL level was decreased in old age group (NDDO) and in diabetic sub groups (DDM and DDO).
4. Age as well as diabetic state was affecting factors of lipid profile.
5. In diabetic patient lipid profile was more severely deranged in older sub group (DDO) as compare to middle aged sub group (DDM).
6. 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.
7. 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

This study was concluded that age as well as diabetic state had deleterious effects on lipid profile. All constituent of lipid profile had an increasing trend with age except HDL which had a negative trend with advancing age; this was true in diabetic and non diabetic subjects as well. Further on the basis of the present study and other evidences regarding the changes in lipoprotein during aging and diabetes mellitus. It may be suggested that diabetes mellitus accelerates age related disturbance in lipid profile.

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