

To Determine the Patterns of Dyslipidaemia Amongst the Macrovascular Complications of Type – II Diabetes Mellitus

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Objective: To assess the characteristics of dyslipidaemia amongst the type 2 diabetic patient with macrovascular complications like ischaemic heart disease, cerebrovascular and peripheral vascular disease and to compare the variables of dyslipidemia in male and female subjects under study.

Design: A prospective observational analytic study.

Setting and place of Study: Study was conducted in medical unit-III of Bahawal Victoria Hospital Bahawalpur, over a period of 6 months from 1st July, 2008 to 31st December, 2008.

Procedure: A total of hundred patients of type 2 diabetes were randomly selected for study. Those who had hyperlipidaemia due to secondary causes e.x. nephrotic syndrome, drugs, hypothyroidism etc. were excluded. Blood samples were taken for serum sugar fasting and random and fasting lipid profile. For statistical analysis student t.test at 5% level of significance was used. All mean values were presented as mean \pm SD (Standard Deviation).

Results: Majority of patients presented in middle and old age category, and they had poor glycemic control. The female patients had uncontrolled hyperglycemic and hypertensive (BP = $145 \pm 25.72 / 85.6 \pm 76$ mm/Hg) than males and their mean random serum sugar was 246.64 ± 105 mg% High percentage of complications were observed in patients of middle age group with great frequency of cardiovascular complications like coronary heart diseases and hypertension (52%) followed by cerebrovascular complications (30%) and peripheral vascular disease (18%). The lipid profile was in high risk range in patients with cardiovascular and cerebrovascular complications. In patients with CHD, the mean \pm SD concentration of cholesterol was 207.08 ± 27.94 mg/dl, HDL – C was 34.8 ± 6.27 mg/dl and TC : HDLC ratio > 6 , (normally TC:HDLC ratio should be < 5 and HDL – C > 40 mg/dl). In patients with CVA, HDL – C was 35.09 ± 6 mg/dl and triglycerides was 146.9 ± 50.70 mg/dl and these variables meet the definition of isolated low HDL – C (defined as TG < 150 mg% and HDL – C < 35 mg% = isolated low HDL – C) and that was considered as independent risk factor. LDL – C concentration was high normal (188 ± 23.4 mg/dl) in these cases. Collectively the mean concentration of LDL-C was raised and statistically very highly significant in all these macrovascular complications. In female patients, the mean concentration of LDL – C, triglycerides and HDL – C was 191 ± 31.6 mg/dl, 179 ± 93 mg/dl and 32 ± 2.4 mg/dl respectively, all in high risk range.

Conclusion: Poor glycemic control is associated with higher incidence of dyslipidaemia in type 2 diabetes. Current study confirms the association of hypercholesterolemia, low HDL-C and increased TC HDL-C ratio (all in high risk range) in patients with coronary heart disease, hypertension and CVA. Lipid profile was found to be significantly higher among females.

Key Words: Diabetic dyslipidaemia HDL – C. LDL – C. Triglycerides. Macrovascular complications.

Introduction

Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to insulin resistance. It is estimated that about 120 million people are affected with diabetes worldwide and this number will grow to 300 million by the year 2025 and majority will be asians.¹ WHO ranks Pakistan 7th on diabetic prevalence list with 6.9 million diabetic people.²

Type 2 diabetes is more prevalent form and it typically occurs in setting of metabolic syndrome which also include obesity, hypertension and hyperlipidemia. The relative insulin deficiency or insulin resistance seen in such patients tend to promote atherosclerosis, the central pathological mechanism of macrovascular complications.^{3,4} Moreover diabetic

dyslipidaemia is believed to be a major cause of increased risk of such complications. It is characterized by increase in LDL and decrease in cardioprotective HDL. LDL become small and dense and more atherogenic than larger buoyant counterpart because they are more likely to oxidize and more readily adhere to arterial wall.⁵

Clinical trials suggest that various pattern of dyslipidemias predispose the patients to macrovascular complications like coronary heart disease, cerebrovascular diseases and hypertension.^{6,7}

Hypertriglyceridemia and high T.C : HDL – C ratio may represent high risk group for coronary heart diseases mortality. It has been observed that better glycemic control and lipid lowering therapy may result in 22% to 24%

reduction in unique cardiovascular events.⁸ The most recent guidelines of National Cholesterol Education Programmed Adult Treatment Panel (NCEP ATP III) consider diabetes as CHD risk equivalent.⁹

Studies have shown that majority of patients with cerebrovascular accident are found to be diabetic and glycemic control being a modifiable risk factor. Hyperlipidaemia have been observed in individuals who suffer from non hemorrhage stroke, but not in those who suffer from cranial or subarachnoid hemorrhage. Similarly lower extremity amputation occurs 10 – 30 times more frequently in diabetic patients as compared to non diabetics and 70% of lower limb amputations occur in people with diabetes.¹⁰

Pakistanis belong to an ethnic group with highest rate of above mentioned complications. Previously few detail studies had been carried out in the area of South Punjab, to determine the prevalence of hypercholesterolemia, hypertriglyceridemia, TC : HDL – C ratio and low HDL – C in this population.

Aims and Objectives of Study

- 1) To analyze patterns of dyslipidemia amongst the macrovascular complications (ischaemic heart disease, cerebrovascular, peripheral vascular disease) of type 2 diabetes mellitus.
- 2) Comparison of different variables of dyslipidemia among male and female subjects under study.

Patients and Methods

This hospital based prospective observational study was carried out in Medical Unit-III of BVH Bahawalpur, Pakistan during 6 months time period from 1st July 2008 to 31st December 2008. Hundred adult type 2 diabetic patients (comprising equal number of males and females), between the age of 30-70 years, were randomly selected in this study. History and clinical examination was recorded on each performa after taking a formal consent. Blood samples were collected after overnight fast, centrifuged within 15 minutes of venopuncture and lipid levels were determined by means of enzyme linked immunosorbent assay kit (Randox Laboratories). The concentration of LDL-C was calculated by using Friedwald formula:

$$LDL - C = TC - HDL - C - TG/5$$

Serum sugar fasting and random was determined by enzymatic color test on spectrophotometer. All these collected data were fed and analyzed through computer software SPSS (Version – 10). Different frequencies were calculated and presented in tabulated form. Mean values of quantitative data were presented as means \pm SD (standard deviation) and all these data was analyzed by a statistician. Student 't' test was applied and values were tested at 5% significance level ($\alpha = 5\%$).

Inclusion Criteria: Patients with following macrovascular complications were included.

- (i) **Coronary Heart Disease:** It was diagnosed by assessment of typical clinical features, radiological and EKG findings and raised cardiac enzymes.
- (ii) **Hypertension:** Based on recommendations of ADA and European guidelines, B.P. > 130 / 80 mm/HG is considered abnormal in diabetics.
- (iii) **Cerebrovascular Accident:** Stroke was defined according to WHO criteria “rapidly evolving symptoms and signs of focal and at time global loss of cerebral functions without apparent cause other than that of vascular origin” and neurological examination along with CAT Scan brain was conclusive.
- (iv) **Peripheral Vascular Disease:** Patients without palpable popliteal, dorsal pedis or posterior tibial on examination with or without history of claudication were labeled as peripheral vascular disease. Doppler ultrasound was conclusive.

Exclusion Criteria: On basis of history and physical examination, those diabetic patients suffering from chronic liver disease, nephrotic syndrome, hypothyroidism or having pregnancy, were excluded. The patients with history of oral contraceptives pills, steroids, β blockers and thiazide diuretics were also excluded.

Defination of Variables of Dyslipidemia: As determined by WHO and American Diabetic Association, for diabetic patients with vascular complications, following variables with their values were considered abnormal for study.^{11,12}

Hypercholesterolemia	= Serum TC > 200 mg/dl OR LDL > 130 mg/dl (It is desirable to keep LDL-C < 100 mg/dl in diabetics)
Hypertriglyceridaemia	= Serum TG > 180 mg%
Isolated low HDL	= HDL – C < 35 mg/dl and TG < 150 mg/dl
Low HDL-C	= HDL < 40mg/dl
TC: HDL ratio	= It is recommended that ratio should be considered < 5

(if ratio is between 5 - 6.5 the risk of myocardial infarction is doubled. If ratio is > 6.5, risk is seven fold).

Results

A data of hundred patients of type 2 diabetes were analyzed. A comparison of clinical and demographic parameters subjects are shown in Table No. 1. This table shows characteristic differential features by gender. Female were found to be hypertensive and obese. Systolic B.P was 135.7 ± 21.29 mm/Hg in male and 145 ± 25.75 mm/Hg in females. While diastolic B.P. was 80.21 ± 13.38 and 85.6 ± 17.6 mm/Hg respectively. The mean blood glucose level in males was 228.57 ± 101.6 mg/dl and 246.64 ± 105.06 mg/dl in females. Both groups showing poor glycemic control and females had more uncontrolled hyperglycemia and also hypertensive.

Table 1: Demographic and Clinical Parameters among Male and Female Subjects.

Variables	Male (n = 50)	Female (n = 50)
Systolic B.P (mmHG)	135.71 ± 21.29 (32%)	145 ± 25.75 (50%)
Diastolic B.P (mmHg)	80.21 ± 13.38 (18%)	85.6 ± 70.60 (27%)
Blood glucose (R) (mg%)	228.57 ± 101.6	246.64 ± 105.66
Weight (kg)	54.39 ± 10.14	56.37 ± 14.75

Table 2 projects the frequency of macrovascular complications and their correlation with characteristic lipid profile. It is apparent that most of patients were suffering from coronary heart diseases (52%) followed by cerebrovascular accident (30%) and peripheral vascular diseases (18%). In patients with CHD, CVA and peripheral vascular disease, the mean concentration of cholesterol was 207.08 ± 27.1 mg/dl

(T – value = 27.94), 188 ± 23.4 mg/dl (T – value = 20.13) and 168.20 ± 19 mg/dl (T – value = 15.23) respectively. All these concentration were raised above normal and statistically very highly significant.

The mean HDL – C concentration was 34.85 ± 6.27 mg/dl (T – value = 5.81) and 35.09 ± 6.78 mg/dl (T – value = 3.97), in patients with CHD and CVA respectively. Both these values were below normal and statistically significant. Again in patients with coronary heart diseases, the LDL-C: HDL-C ratio was 6.0 and high risk range.

Table 3 shows the comparative values of lipid profile among male and female subjects. In female patients the mean values of triglycerides, LDL-C and HDL-C was 179 ± 93 mg/dl, 191 ± 31.6 mg/dl (T – value = -2.01 significant), 32 ± 2.4 mg/dl (T – value = -23.57 very highly significant) and T.C: HDL-C ratio was 5.3 (raised). In males the mean concentration of triglycerides, LDL – C and HDL – C was 165 ± 49 mg/dl (T – value = -2.16), 177 ± 41 mg/dl (T – value = 13.2) and 35.2 mg/dl (T – value = -6.53) respectively and all these values were statistically significant. Although the lipid profile was elevated in both groups, it was more in high risk range in females as compared to males.

Table 2: Frequency of Macrovascular Complication and the Comparison with Characteristic Lipid Profile.

	Frequency	Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL – C (mg/dl)	LDL : HDL – C Ratio
Coronary Heat Disease	N = 52	207.08 ± 27.1 (T – Value = 27.94)**	175.5 ± 38.4 (T – Value = -.82)	34.85 ± 6.27 (T – Value = -5.81)*	6.0
CVA	N = 30	188 ± 23.4 (T – Value = 20.13)**	146.91 ± 50.70 (T – Value = -3.57)*	35.09 ± 6.78 (T – Value = -3.97)*	5.2
Peripheral Vascular Disease	N = 18	168.20 ± 19 (T – Value = 15.23)**	171.2 ± 40.49 (T – Value = -.92)	38.6 ± 5.43) (T – Value = -1.09)	4.5

* Significant

** Highly Significant

Table 3: Mean and Standard Deviation of Lipid Concentration, Affected by Gender.

Lipid Concentration (mg/dl)	Males N=50	Females N=50
Triglycerides	165±49 (T-Value=2.16)**	179±93
LDL –C	177±41 (T-Value= 13.28)*	191±31.6 (T-Value= -2.01)*
HDL –C	35.2±5.2 (T-Value= -6.53)**	32±2.4 (T-Value= 23.57)***
TC : HDL Ratio	4.7	5.3

* Significant
** Highly Significant
*** Very Highly Significant

Discussion

This study showed that most patients of type 2 diabetes presented in middle and old age group with mean duration of 5 years. As far as the characteristic clinical parameters between male and females are concerned, our results showed that females are hypertensive and heavier than males. 50% of females had systolic and 18% diastolic hypertension. Mean concentration of glucose, triglyceride and LDL cholesterol was significantly elevated and HDL – C in high risk range in females as compared to males. These results are in conformity with those reported by Talat Naheed et.al¹³ and Sohail Rafiq et.al.¹⁴ They have also concluded that plasma lipids were higher in females with poor glycaemic control. After menopause the diabetic females develop atherosclerosis much faster. This may explain the four fold increase risk of coronary heart disease and hypertension in diabetic females.

The above mentioned findings are in contrast to another study held in Rawalpindi region which showed that diabetes was more prevalent in males and also males had dyslipidemia along with poor glycaemic control.¹⁵

The frequency of macrovascular complications appear to be strongly related to duration of disease and poor glycaemic control. In our study 50% of patients had CHD and hypertension followed by CVA (30%) and peripheral vascular disease (18%). In a large multicentre cross-sectional survey, Khawaja AK et.al¹⁶ has similarly estimated that over 50% of diabetic patients with macrovascular complication had coronary heart disease and the rest in accounted for CVA and peripheral vascular disease.

Interestingly the lipid profile of present study has revealed statistically significant elevated level of serum cholesterol, low HDL – C and increase TC : HDL – C ratio in our patients of coronary heart disease, hypertension and CVA. Our data are in conformity with a similar study conducted in Multan region by Ahmad Abrar et.al.¹⁷ They have reported increased prevalence of LDL-C, Low HDL-C and abnormal TC : HDL ratio in diabetic patients with CHD and CVA.

It is also important to compare that baseline mean HDL – C levels in our study are well below the normal levels (40 mg/dl) and LDL – C above normal (100 mg/dl) recommended by National Cholesterol Education Program.⁹ Infact this “atherogenic dyslipidemia” observed in our study show a significant association with CHD and CVA.

Our above mentioned results are also verified by several major randomized control trials. UKPDS, with the aim to compare lipoproteins amongst type 2 diabetes, also showed that lipid concentration increase with age. It also observed that serum cholesterol was raised and HDL was low in diabetic females with macrovascular complication.¹⁸

The finding of increased TC : HDL – C ratio in our patients of coronary heart diseases in line with a large population heart protection study. It showed that if ratio is between 5 to 6.5, the risk of myocardial infarction is doubled and if ratio is >6.5, risk is seven fold.^{19,20}

Conclusion

Diabetic dyslipidemia in modifiable risk factor and important cause of morbidity. Poor glycaemic control is associated with higher incidence of dyslipidemias. We conclude the significant association of hypercholesterolemia and low HDL – C in patients with CHD, CVA and peripheral vascular disease. The present study also confirms the high TC: HDL – C ratio as coronary risk.

Generally in South East Punjab, the health care providers should educate the patients about preventive measures of these potential complications and it will contribute to ultimate better outcome.

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