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FREQUENCY OF DYSLIPIDEMIA IN PATIENTS HAVING TYPE 2 DIABETES MELLITUS PRESENTING TO MEDICAL OPD/EMERGENCY IN KHYBER TEACHING HOSPITAL PESHAWAR

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ABSTRACT

Background: Dyslipidemia is an important modifiable risk factor for cardiovascular disease among patients of type 2 diabetes mellitus. Timely detection and characterization of this condition help clinicians estimate future risk of cardiovascular disease and take appropriate preventive measures. The aim of this study was to determine the prevalence of dyslipidemia in a cohort patient with type 2 diabetes mellitus presenting to OPD/emergency in department of General Medicine in Khyber Teaching Hospital Peshawar.

MATERIAL AND METHODS: A cross sectional descriptive study was conducted among the patients of Type 2 Diabetes mellitus presenting to OPD/emergency in department of General Medicine in Khyber Teaching Hospital Peshawar. The study was conducted from January 2022 to June 2022 over a period of six months. All

Results: I found mixed dyslipidemia as the most prevalent (88.1%) and isolated dyslipidemia (10.1%) as the least prevalent forms of dyslipidemia in our patients. The most prevalent form of single dyslipidemia was high LDL-C (73.8%) and combined dyslipidemia was high TG, high LDL-C and low HDL-C (44.7%). Prevalence of all single and mixed dyslipidemia was higher in patients with poor glycemic control and hypertension. The glycemic status of patients correlated with their fasting serum lipid profile. Dyslipidemia was associated mainly with male gender, poor glycemic control and hypertension

Conclusion: It shows that dyslipidemia is associated mainly with male gender, poor glycemic control and hypertension. It is highly prevalent in patients with type 2 diabetes. Urgent lifestyle modification, sustained glycemic control and aggressive lipid lowering treatment plans are necessary to minimize the future risk of cardiovascular disease in this population

Key words: Dyslipidemia, Type 2 Diabetes Mellitus, Khyber Teaching Hospital, Peshawar

INTRODUCTION:

Type 2 diabetes mellitus (T2DM) is the third major non-communicable disease in Pakistan, and is approaching pandemic levels due to rapid change in socioeconomic status and life-style of the people.[1] T2DM amplifies the risk of cardiovascular disease (CVD) several fold, making it a significant risk factor of the latter. More than 50% patients with T2DM die due to coronary heart disease (CHD).[2] Among several modifiable and non-modifiable risk factors for CVD, T2DM is the strongest, as it is strongly associated with atherogenic dyslipidemia.[3] The atherogenic dyslipidemia in diabetic patients results from insulin deficiency or resistance that promotes lipolysis in the visceral adipocytes and increases the flux of free fatty acids in plasma and liver. Moreover, the activity of an endothelial enzyme, lipoprotein lipase, also decreases.[4] These conditions lead to hepatic steatosis, over-secretion of larger triglyceride (TG)-rich very low density lipoprotein 1(VLDL1) particles into the plasma, over-secretion of hepatic apolipoprotein B (ApoB), impaired clearance of chylomicrons and decreased receptor mediated endocytosis in the liver.[5] The most common phenotypic pattern of diabetic dyslipidemia involves lipid triad with raised triglycerides, reduced high density lipoprotein cholesterol (HDL-C) and increased concentration of small, dense low density lipoprotein cholesterol (LDL-C) particles.[6] Additionally, total cholesterol (TC)/HDL-C ratio, non-HDL-C and ApoB have also been shown to be directly involved in the atherogenic process and development of CVD.[7] Diabetic dyslipidemia has therefore emerged as an important biomarker for the increased CVD risk observed in diabetic patients. Significant reduction of CVD related morbidity and mortality by lipid-lowering agents such as statins underscores their importance in the cardiovascular health of diabetic patients.[8] Therefore, early detection and aggressive management of dyslipidemia are very important in saving the lives of diabetic patients from atherogenic cardiovascular diseases.

The Western hilly region of KPK is mostly populated by ethnic groups like tribals which differentiates this population genetically from other areas of Pakistan. The socioeconomic status, life-style, dietary habit and cultural practices of these ethnic groups make them more vulnerable to high incidence of CVD than any other ethnic groups in this region. [9] Few recent hospital based studies and our own clinical observations have shown that the prevalence of metabolic syndrome and cardiovascular disease is very high in this region particularly among these ethnic groups.

However, no systematic study has been carried out so far in this region to map the actual epidemiology of CVD risk factors including the dyslipidemia. Given that the prevalence and pattern of CVD risk factors differ according to geographic location, ethnicity, dietary habits and socio-economic status of the population under study, we hypothesize that epidemiology of dyslipidemia is different for the population of this region compared to others. Our study thus aims to describe the prevalence, pattern and independent predictors of dyslipidemia among type 2 diabetic patients of Western hilly region of KPK. This study will help us to determine the frequency of dyslipidemia in patients with type 2 diabetes mellitus in our local population.

OBJECTIVE:

To determine the frequency of dyslipidemia in patients with type 2 diabetes mellitus presenting to OPD/emergency in department of General Medicine in Khyber Teaching Hospital Peshawar (KTH).

MATERIAL AND METHODS:

A descriptive cross sectional study was conducted among patients with type 2 diabetes mellitus presenting to OPD/emergency in department of General Medicine in Khyber Teaching Hospital Peshawar. The study was carried out from January 2022 to June 2022 over a period of six months. Using WHO sample size calculated, sample size was calculated to be 102, keeping the prevalence of dyslipidemia 81.8%, with 95%. Non-probability consecutive sampling was used for the collection of data. All patient with age ranging from 30-70 years, both genders and suffering from Type-2 Diabetes for more than one year were included in the study after taking inform written consent, assuring the confidentiality of the data to the participants. Among consented patients, those

with a history of nephrotic syndrome, hypothyroidism, end stage renal disease, on certain medications like thiazide diuretics, oral contraceptives, and corticosteroids or already on lipid lowering drugs were excluded from the study to minimize selection bias.

Data collection procedure: 165 patients fulfilling the inclusion criteria from outdoor Department of Medicine, KTH, Peshawar were included in the study after permission from ethical committee and research department of Khyber Teaching Hospital. Basic demographics like age, gender, weight on weighing machine, duration of diabetes were recorded. A 3 ml of Venous blood sample was collected from the patients, after an overnight fasting of 8 hours. Serum sample were analyzed for parameters like serum lipids which include total cholesterol, triglycerides, high density lipoprotein (HDL) and LDL. For all investigations of patients Khyber teaching hospital main pathology laboratory was used. Type 2 diabetes was defined as having fasting plasma glucose concentration > 126mg/dl on two different occasion two days apart on laboratory test providing not taken medications or insulin. While Dyslipidemia was defined as High Density Lipid cholesterol (HDL-C) < 40 mg/dl, Triglyceride (TG) >150mg/dl, Low Density Lipid cholesterol (LDL-C) > 130 mg/dl and Total cholesterol (TC) >200 mg/dl.

Data analysis: Data was analyzed with statistical analysis program (SPSS-V.22). Frequency and percentage were computed for qualitative variables like gender, family history of dyslipidemia and dyslipidemia. Effect modifiers like age, gender, duration of diabetes, weight and height of the patient in order to calculate the BMI, family history of dyslipidemia, duration of illness and severity of dyslipidemia were controlled by stratification. Post stratification chi square test will be applied p ≤0.05 will be considered statistically significant.

RESULTS

A total of 165 type 2 diabetic patients, 36.2% females and 63.8% males, were enrolled in the defined study, where the mean age of the patients was 52.7 ± 10.5 years. The patients were stratified on the basis of BMI in to three categories as shown in the Table1 below. The mean diabetes duration was 5.1 ± 3.8 years among both males and females. Among these, 53 (35.4%) patients were not taking any anti-diabetic drugs, 72 (56.7%) were taking only oral hypoglycemic drugs, 26 (5.2%) were taking both oral hypoglycemic drugs and insulin, and remaining 14 (2.6%) were taking only insulin for controlling their blood glucose levels. Their demographic, anthropometric and biochemical characteristics are presented in Table 1. Males were significantly (p < 0.010) older, overweight or obese than females. Majority of the patients were urban residents (74.2%). Prevalence of smoking habit (36.9%), general obesity (36.3%) and central obesity (51.7%) was significantly higher in males than in females (p < 0.010). There were 24.1% patients with poor glycemic control (HbA1c > 7.0%). The fasting plasma glucose level, duration of diabetes and hypertension, glycemic status and blood pressures did not differ significantly between males and females (p > 0.050).

Table 1: Demographics of the patients

		Gender		P value	Total
		Male	Female		
Age (years)		53.56 ±11.97	55.32±9.07	0.326	54.20 ± 11.008
BMI (kg/m^2)		24.33±2.12	30.40±2.96	0.000	26.54 ±3.818
BMI Groups	≤ 24	56(100.00%)	0(0.00%)	0.000	56 (100%)
	24.01-27.00	41(83.67%)	8(16.33%)		49 (100%)
	>27	8(13.33%)	52(86.67%)		60 (100%)
Waist circumference (cm)		95.18±7.25	89.15±7.98	0.000	92.99 ± 8.046
Residence	Mountain	27(62.79%)	16(37.21%)	0.894	43 (100%)
	Urban	78(63.93%)	44(36.07%)		122 (100%)
Fasting Blood Sugar		132.84±44.79	136.23±42.32	0.633	134.073 ±

					43.8111
Duration of Diabetes (years)		4.67±3.24	6.40±3.86	0.002	5.297 ± 3.56512
HbA1c		6.30±.98	6.55±1.05	0.118	6.39 ± 1.00631
HbA1c groups	≤7	83(66.40%)	42(33.60%)	0.196	125 (100%)
	>7	22(55.00%)	18(45.00%)		40 (100%)

Among all the measured lipid parameters, only the serum TG level was higher in males ($p < 0.050$). Age is a major confounding factor for dyslipidaemia, the analysis showed that serum TG and HDL-C levels decreased while other lipid parameters increased with age. Gender-wise analysis showed that such age-specific variation of serum lipid parameters was more obvious in males than in females. Serum lipid levels and ratio were either unchanged or decreased with age in female patients. A one-way between-groups analysis of variance was conducted to explore the impact of age on serum lipid parameters. The difference in concentrations and ratio of serum lipid parameters for the three age groups (30–44, 45–59 and 60–74 years) was statistically significant except for TG. Serum LDL-C concentration and TC/HDL-C ratio of age group 45–59 years differed from either age groups while serum concentrations of TC and non-HDL-C differed only with age group 30–44 years. No age group specific variation was found in the serum lipid parameters for females. In males, the serum concentrations of TC, LDL-C, non-HDL-C, and TC/HDL-C ratio of age group 30–44 years differed significantly from age groups 45–59 and 60–74 years. Only LDL-C concentration of age group 45–59 years differed significantly from age groups 30–44 and 60–74 years. Serum TC, non-HDL-C and TC/HDL-C ratio of age group 45–59 years differed significantly only from age group 30–44 years. Prevalence of single and mixed dyslipidaemia has been presented in Table 2. The most prevalent single lipid disorder was increased non-HDL-C (75.5%) while the least prevalent was hypercholesterolemia (43.7%). Prevalence of mixed dyslipidaemia was 88.1%. Prevalence of high LDL-C, non-HDL-C, ApoB and mixed dyslipidaemia was significantly higher among males ($p < 0.05$).

Table 2 Age-and sex specific prevalence of single and mixed dyslipidemia in diabetic patients.

		Age Groups (total)				Gender						P value
		30-44	45-59	60-74	P value	Male			Female			
						30-44	45-59	60-74	30-44	45-59	60-74	
Hypertriglyceridemia	Yes	21	48	39	0.255	19	28	23	2	20	16	0.66
	No	8	33	16		5	19	11	3	14	5	
Hypercholesterolemia	Yes	8	39	23	0.147	7	24	15	1	15	8	0.63
	No	21	42	32		17	23	19	4	19	13	
Low HDL-C	Yes	16	31	29	0.139	13	18	17	3	13	12	0.90
	No	13	50	26		11	29	17	2	21	9	
High LDL-C	Yes	24	56	40	0.345	20	34	26	4	22	14	0.19
	No	5	25	15		4	13	8	1	12	7	
High TC/HDL-c ratio (%)	Yes	15	29	30	0.069	14	15	19	1	14	11	0.76
	No	14	52	25		10	32	15	4	20	10	
Mixed dyslipidemia	Yes	25	75	51	0.377	21	45	32	4	30	19	0.27
	No	4	6	4		3	2	2	1	4	2	

Table 3 presents the prevalence of single and mixed dyslipidemia in diabetic patients based on their characteristics such as duration of diabetes, place of residence, smoking habit, glycemic status and blood pressure. Prevalence of low HDL-C and high TC/HDL-C ratio was significantly higher ($p < 0.050$) in patients with longer duration of diabetes. The prevalence of hypertriglyceridemia,

High LDL-C and Mixed dyslipidaemia were significantly higher ($p < 0.050$) in non-smoker patients.

Table 3: Prevalence of single and mixed dyslipidemia in diabetic patients based on various characteristics of diabetic patients

	High TG (%)	High TC (%)	Low HDL-C (%)	High LDL-C (%)	High TC/HDL-C (%)	High non-HDL-C (%)	Mixed dyslipidemia (%)
BMI (kg/m^2)							
<25	58.8	40.9	43.0	70.9	42.4	73.3	83.1
≥25	74.4	49.4	47.5	80.0	51.3	80.0	92.5
p value	0.001	0.077	0.212	0.031	0.065	0.105	0.005
Duration of DM (years)							
≤7	64.4	40.8	39.7	73.6	40.8	77.2	86.4
7–13	61.0	49.6	56.9	74.0	56.9	69.9	85.4
≥14	71.4	64.3	57.1	78.6	57.1	78.6	85.7
p value	0.656	0.069	0.016	0.917	0.006	0.257	0.960
Place of residence							
Rural	65.6	46.9	42.2	77.3	43.8	79.7	87.5
Urban	63.1	42.5	45.3	72.6	45.8	74.0	85.6
p value	0.615	0.395	0.691	0.296	0.688	0.196	0.599
Current smoker							
No	71.9	41.5	45.2	73.3	50.4	74.8	85.9
Yes	28.1	59.5	55.8	27.7	49.6	26.2	14.1
P Value	0.015	0.395	0.917	0.296	0.388	0.946	0.569

DISCUSSION:

The aim of the study was to determine the prevalence dyslipidemia in a cohort of type 2 diabetic patients from a teaching hospital of Western hilly region of Pakistan. We found that the majority of the patients had higher levels of serum TG, TC, non-HDL-C, ApoB and TC/HDL-C ratio and lower level of serum HDL-C than the cut off values recommended by the NCEP ATP III.[2] Abnormal lipid profiles in our diabetic patients were not surprising. Insulin resistance or deficiency leads to increased rate of lipolysis in adipocytes and influx of free fatty acids into the liver resulting into overproduction of triglyceride rich lipoproteins. Moreover there is delayed clearance of such lipoproteins due to decreased activity of the endothelial bound enzyme lipoprotein lipase.[10] There was no significant difference between the serum levels of these lipid parameters between males and females except for serum TG, which is in agreement with previous hospital and population based studies in Asian, African, European and North American type 2 diabetic populations.[11] Some studies have also shown higher levels of atherogenic lipid profile in women[12] but such different outcomes may have resulted from differences in age distribution, treatment status for diabetes and dyslipidemia, glycemic status, duration of diabetes and nature of study population.

Age is a non-modifiable risk factor for CVD, the effect of age on serum lipid profile among our patients, we report a rise in the serum levels of TC, LDL- C, non-HDL-C and TC / HDL-C ratio with increasing age of patients and a gradual fall in serum TG and HDL-C levels. Several cross-sectional and longitudinal studies conducted elsewhere have also shown similar results.[13,14] The plasma level of lipids is determined by the balance between synthesis and removal of lipoprotein particles. Ageing causes increased TC and LDL-C levels due to impaired clearance from plasma through reduced expression of hepatic LDL-C receptor.[15] Similarly, age-associated rise in ApoB has been shown to be the result of an increased production of VLDL ApoB-100 and decreased clearance rate of LDL-C ApoB-100.[16] Plasma TG levels were expected to be higher in older patients, but this was not observed in our study. The unexpected decline of plasma TG level with the advancing age could partly be due to masking effect of treatment of certain old age patients with insulin and lipid lowering drugs. Moreover, menopause has been shown to be an additional risk factor in older women that significantly decreases plasma HDL-C and increases LDL-C levels.[17] Age related decline in HDL-C levels likely results from insulin resistance, inflammation, hormonal decline, cellular senescence and ageing of the HDL-C particle itself, affecting HDL-C formation.[18] This explains the increased prevalence of atherogenic dyslipidemia and risk of CVD with age. Our study has confirmed previous findings that serum lipid parameters are highly correlated with fasting blood glucose and HbA1C, irrespective of the population studied.

We further observed moderate to strong correlation of primary lipid parameters such as TC, HDL-C, and LDL-C with derived or secondary lipid parameters such as TC/HDL-C ratio and non-HDL-C which are regarded as better predictors of insulin resistance, metabolic syndrome and CVDs.[19] There are some studies from other parts of KPK that have reported varying prevalence and pattern of dyslipidemia in type 2 diabetic patients.[20] The latest prevalence of mixed dyslipidemia was 63.8% in eastern Pakistan, 61.0% in central KPK and 90.7% in mid-western KPK. The most prevalent single dyslipidemia in both central and mid-western Nepal was low HDL-C.[21] The least prevalent single dyslipidemia was hypercholesterolemia in central Nepal and high LDL-C in KPK. Our study provides the first detailed report on the prevalence and pattern of dyslipidemia in diabetic population from tribal zones of western kpk. We found high prevalence of dyslipidemia in our patients, with mixed dyslipidemia being the predominant type. The most prevalent primary single dyslipidemia was high LDL-C while hypercholesterolemia was the least prevalent. Three quarters of the patient population showed high non-HDL-C. High LDL-C was the only isolated dyslipidemia present in our patients. The typical atherogenic dyslipidemia was present in about half of the patients.

Males had significantly higher prevalence of high LDL-C, high non-HDL-C and mixed dyslipidemia than females, while other lipid parameters were similar. This is in agreement with previous reports from Nepal and elsewhere.[22] We found age specific increase in prevalence of dyslipidemia only in males, with females showing stable or decreasing prevalence with age. Our findings are in agreement with previous reports.[23] The age-specific variation in the prevalence of dyslipidemia is believed to be due to age-related decline in sensitivity of peripheral tissues to insulin and increase in metabolic disorders of carbohydrates and lipids.[24] This effect could have been masked in our female patients because of better control of their diabetes. We also analyzed the effect of other modifiable risk factors of CVD on the prevalence of dyslipidemia.

We did not find significant difference in prevalence of dyslipidemia between smoker and non-smoker patients except for hypertriglyceridemia. This lack of difference could be due to inclusion of relatively low number of smokers (27.2%) as compared to non-smokers (72.8%). Another possibility is that the intensity of smoking was low in these smokers and some of the non-smokers may have been recent ex-smokers. Studies have shown that intensity of smoking is associated with small but significant increases in LDL-C and decreases in HDL-C while smoking cessation is associated with improvement in HDL-C, total HDL and large HDL particles, especially in women.[25] As expected, we found significantly higher prevalence of hypertriglyceridemia, low HDL-C, high LDL-C, high TG/HDL-C ratio and mixed dyslipidemia in patients with poor glycemic control and

hypertension. Moreover, prevalence of low HDL-C and high TC/HDL-C ratio was also higher in patients with longer duration of diabetes. These findings are in agreement with the findings of many other studies conducted among diabetic patients in other populations.[26] Type 2 diabetes is often associated with the cluster of several other risk factors of CVD such as older age, insulin resistance, obesity, hypertension, poor glycemic status, microalbuminuria, alterations in inflammatory, coagulation and thrombolytic markers in addition to the atherogenic dyslipidemia.[27]

We also explored the covariate risk factors that were independently associated with dyslipidemia in our patients. Age group ≥55 year, current smoking habit, fasting hyperglycemia, poor glycemic control and hypertension were found to be strongly associated with hypertriglyceridemia. Fasting plasma glucose, hypertension and its duration were associated with hypercholesterolemia. Low HDL-C was associated with male gender, central obesity and fasting plasma glucose. High LDL-C was positively associated with male gender and fasting plasma glucose. High non-HDL-C and ApoB were independently associated with male gender, fasting plasma glucose, poor glycemic control and hypertension. High ApoB was also found to be associated with longer duration of hypertension. These risk factors are recognized by many international guidelines and remain the targets for preventing CVDs among diabetic patients. As dyslipidemia is a well-established risk factor for cardiovascular diseases, presence of other co-variate risk factors results significantly higher risk of future CVD. This is in agreement with our earlier studies which have estimated higher risk of 10-year CHD among type diabetic patients.[28] These findings warrant extensive preventive approaches, both clinical and non-clinical, to treat all types of dyslipidemia to minimize the future risk of CVD in our patients. **CONCLUSION:**

The study provides the first detailed report of prevalence of dyslipidemia in type 2 diabetic patients attending a tertiary care hospital of western hilly region of Pakistan. It has shown an alarmingly high prevalence of dyslipidemia. Mixed dyslipidemia is more prevalent than combined or single dyslipidemia. The prevalence of dyslipidemia was found to be strongly associated with various co-variate risk factors of CVD such as old age, male gender, smoking, poor glycemic control, obesity and hypertension suggesting high risk of future CVD. Our study therefore contributes to the epidemiology of diabetic dyslipidemia from the Western hilly region of KPK and serves as supportive data for health policy planners to formulate and implement policies that aim to increase public awareness about diabetic dyslipidemia, healthy diet and life-style among diabetic patients and health care providers. It also highlights the need of regular monitoring of blood glucose and lipid profile, aggressive lifestyle changes such as weight reduction and physical exercise and effective medication with anti-diabetic and lipid lowering drugs to obtain proper glycemic control and lipid profile. However, a population based nationwide survey is still warranted to reflect the actual epidemiology of diabetic dyslipidemia in KPK as no such studies has been carried out so far.

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