

DEGREE OF DYSLIPIDEMIAS IN CASES OF TYPE 2 DIABETES MELLITUS WITH AND WITHOUT NEPHROPATHY AT PAF HOSPITAL ISLAMABAD

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Abstract

Background: Dyslipidemia is one of the key contributors to increase morbidity and mortality in type-II diabetes. Presence of diabetic nephropathy is said to further enhance dyslipidemia. Understanding this association can benefit our therapeutic goals in these patients.

Objective: To compare the degree of dyslipidemia in cases of type 2 diabetes mellitus with and without nephropathy.

Material and Methods: This cross-sectional study was conducted at the Department of Medicine, PAF Hospital Islamabad, Pakistan from Mar 2023-Aug 2023. A total of 100 Type 2 Diabetes patients, diagnosed with nephropathy were included in the study group. Another 100 patients with Type 2 diabetes without nephropathy were added in the control group. Biochemical investigations were conducted for both the groups including complete lipid profile, serum albuminuria and serum creatinine. The primary outcome was set as the significance of difference in lipid profile between the two groups.

Results: The mean age in this study was 55.23±8.99 years. The male gender was 67(54%) while female gender was (53) 46% in overall study population. Dyslipidemia was significantly more common in the study group than controls (78% vs. 53%, p<0.001). The study group had significantly higher mean levels of total cholesterol (p < 0.0001), triglycerides (p < 0.0001), LDL cholesterol (p < 0.0001), and VLDL cholesterol (p < 0.0001), while HDL cholesterol showed no significant difference (p = 0.42).

Conclusion: Diabetic patients with nephropathy displayed a markedly higher degree of dyslipidemia, with significantly raised total cholesterol, LDL, triglycerides, and VLDL levels.

Keywords: Dyslipidemia, Nephropathy, Type 2 Diabetes Mellitus.

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Introduction:

Diabetes mellitus (DM) is a condition that is caused by lack of insulin secretion or action and result in elevated levels of glucose in the blood.¹ DM leads to path physiological changes which are then responsible for micro and macro vascular complications causing target organs damage.² One among these micro vascular complications is diabetic nephropathy (DN) which is marked by renal insufficiency progressing in shape of Microalbuminuria and proteinuria.

DN is an independent marker of cardiovascular (CV) events and CV mortality.³ The major cause of vascular complications in diabetes is inflammation of the endothelium caused by a variety of factors like hyperglycemia, activation of RAS system, advanced glycated end products, oxidative stress and oxidation of low density lipoproteins (LDL). Poor glycemic control is however found to be independent risk factor for DN

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explained by the hexamine pathway, polyol pathway and production of advanced glycated end products. The risk of atherosclerotic CV disease (ASCVD) is significantly increased in patients with diabetic kidney disease (DKD), as besides diabetes being a risk factor, DKD causes a variety of complication including severe dyslipidemia.^{4,5}

It is documented that with the progression of DN, there are significant changes in plasma lipid metabolism which causes lipid deposition. The lipoproteins are taken up by epithelial cells and mesangial cells through their unique receptors. It has been demonstrated that the presence of modified LDL in mesangial matrix allow their activation as macrophages. These modified lipoproteins play their role in the pathophysiology of glomerulosclerosis in diabetic patients. The lipoproteins activate adhesion molecules and chemotactic factors issued by mesangial cells and macrophages are hence engaged. Infiltration of monocytes is the result of these processes which then take part in glomerulosclerosis. This is a vicious circle as the macrophages are involved in oxidization of more LDL and nephropathy is aggravated.^{5,6}

In diabetic patients, impaired lipoprotein metabolism, termed 'diabetic dyslipidemia' is characterized by increased levels of total cholesterol (TC), triglyceride (TG), LDL cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and decreased levels of high density lipoprotein cholesterol (HDL-C).^{5,6,7} Insulin resistance present in diabetic patients results in the mobilization of

free fatty acids from the adipose tissue to the liver which leads to increased production of TG. Prolonged diabetes would further raise TG levels, resulting in the accumulation of large TG-rich VLDL particles generating small dense LDL (sdLDL) particles. Imbalance of lipid concentration in the blood (like TG and cholesterol) is said to be present in the early stages of nephropathy and enhances the course of kidney injury. Lipoprotein measurements therefore help to evaluate the progression of DN.⁸

As discussed above, driven mainly by the increased levels of blood glucose, dyslipidemia results in the development of DN.^{9,10,11} Therefore diabetic dyslipidemia and DN are found to be greatly associated with each other and have a major role in future progression of the diabetic related complications progressing towards end stage renal disease (ESRD) and CV events.^{11,12}

This association between of DN and diabetic dyslipidemia is discussed in global literature; however, studies on this topic in Pakistani population are limited. The purpose of this study was therefore to find the difference between serum lipid profile of type 2 diabetic patients with nephropathy and without nephropathy in our local population. The results of this study will help the physicians and endocrinologists to establish evidence based recommendations for optimal management of diabetic patients in our population, helping to prevent future complication of diabetes.

Exclusion criteria were set as patients having urinary tract infection (UTI), end stage renal disease (ESRD), coronary artery disease (CAD), hematuria or thyroid dysfunction.

Biochemical investigations were conducted for both the groups including Glycosylated hemoglobin (HbA1c), TC, LDL-C, TG, VLDL-C, HDL-C, serum albuminuria and serum creatinine as per standard procedures. The primary outcome was set as the significance of difference in lipid profile between the two groups.

Dyslipidemia was labeled when levels of one or more among TC (> 200 mg/dl), TG (≥ 150 mg/dl) or LDL (≥ 100 mg/dl) were above or that of HDL below the targets (≤ 40 mg/dl in males and ≤ 50 mg/dl in females) as set by American Diabetes Association.

Serum creatinine levels were investigated and GFR was calculated with Cockcroft-Gault equation.

A written consent was taken from the patients for the participation in study. Permission for conducting study was taken from the ethical committee, of the Hospital.

Data were analyzed using SPSS version 25. Descriptive statistics were used to summarize baseline characteristics, with means and standard deviations calculated for continuous variables and frequencies with percentages for categorical variables. To control for potential confounders, the results were stratified based on duration of diabetes

Material and Method:

Study Design & Setting:

This hospital based cross-sectional study was conducted at the Department of Medicine, PAF Hospital Islamabad, Pakistan from March 2023 to August 2023 over a period of six months.

Sample Size

Sample size was calculated using WHO sample size software with following assumptions:

Alpha = 5 % (two sided), power = 80%.

p1 (Prevalence of dyslipidemia in diabetic patients with nephropathy) = 75.28%,

p2 (Prevalence of dyslipidemia in diabetic patients without nephropathy) = 56.52%.¹³ Estimated sample size $n_1=100$, $n_2=100$.

Patient's enrolment and sampling Technique:

A total of 100 Type 2 Diabetes patients above the age of 18 years, diagnosed with nephropathy reporting at OPD of the department were included in the study group. Another 100 patients with Type 2 diabetes without nephropathy were added in the control group. To minimize confounding effects, participants in both groups were matched for age, gender, and use of lipid-lowering medications at the patient's enrolment stage.

Exclusion Criteria

(>10 years). Normality of continuous data was assessed using the Shapiro-Wilk test, and all lipid profile parameters were found to be normally distributed. The lipid profile parameters between the two groups were compared using the independent t-test for normally distributed continuous variables, while the Chi-square test was applied for categorical variables such as the presence or absence of dyslipidemia. A p-value of ≤ 0.05 was considered statistically significant for all these comparisons.

Results:

The mean age in this study was 55.23 ± 8.99 years with an age range of 38 to 72 years. The ratio of male gender was 54% while female gender was 46% in overall study population. The group wise details of demographics and clinical findings showed that the duration of diabetes was significantly longer in the study group ($p=0.03$). Similarly, creatinine levels and eGFR were significantly higher in the study group ($p<0.001$ for both), confirming nephropathy status as shown in table-I.

Demographics and clinical findings				
		Study Group n=100	Control Group n=100	p-value
Age (Mean $\pm$ SD) years		56.67 $\pm$ 8.94	55.53 $\pm$ 9.05	0.37
Gender	Male n (%)	55 (55)	53 (53)	0.78
	Female n (%)	45 (45)	47 (47)	
Duration of Diabetes (Mean $\pm$ SD) years		12.14 $\pm$ 3.44	11.52 $\pm$ 3.31	0.19
Body Mass Index Mean $\pm$ SD)		29.25 $\pm$ 4.24	28.66 $\pm$ 3.14	0.26
Family History of Diabetes n (%)		52 (52)	47 (47)	0.48
Medication	OADn (%)	85 (85)	87 (87)	0.68
	Insulin (%)	22 (22)	17 (17)	0.37
	OAD+Insulin (%)	7 (7)	4 (4)	0.35
	Lipid Loweringn (%)	46 (46)	40 (40)	0.39
	ACEI n (%)	39 (39)	35 (35)	0.55
Creatinine(Mean $\pm$ SD) mg/dL		1.42 $\pm$ 0.17	1.16 $\pm$ 0.23	<0.001
eGFR (mL/min/1.73 m ²)		72.55 $\pm$ 13.16	83.48 $\pm$ 8.56	<0.001
HbA1C		9.22 $\pm$ 1.46	9.05 $\pm$ 1.15	0.36

The outcome of the study showed that the frequency of patients with dyslipidemia was significantly higher in the study group compared to the control group (78% Vs. 53% respectively, $p<0.001$). Frequency of patients with lipid abnormalities of different lipid parameters showed higher frequencies of elevated TC ($p<0.0001$), LDL-C ($p<0.0001$), and TG ($p<0.0001$) in the study group compared to the

control. Low HDL-C was more common in the study group however, this difference did not reach statistical significance ($p=0.09$) as shown in Table-II.

Prevalence and major parameters	Study Group n=100	Control Group n=100	p-value/Chi-square
Incidence of dyslipidemia n (%)	78 (78)	53 (53)	<0.001/13.83
Raised Total Cholesterol n (%)	72 (72)	35 (35)	<0.0001/27.52
Raised LDL Cholesterol n (%)	38 (38)	6 (6)	<0.0001/29.84
Raised triglycerides n (%)	74 (74)	47 (47)	<0.0001/15.25
Lowered HDL Cholesterol n (%)	52 (52)	40 (40)	0.09/2.89

The study group had significantly higher mean levels of TC ($p < 0.0001$), TG ($p < 0.0001$), LDL-C ($p < 0.0001$), and VLDL-C ($p < 0.0001$), while HDL-C showed no significant difference ($p = 0.42$), as shown in Table-III.

Study Outcomes	Study Group n=100	Control Group n=100	95% CI	p-value
Total cholesterol (mg/dL)	217.05 $\pm$ 25.03	194 $\pm$ 25.48	16.15 to 29.95	<0.0001
Triglycerides (mg/dL)	179.3 $\pm$ 31.38	145.3 $\pm$ 19.94	26.67 to 41.33	<0.0001
LDL Cholesterol (mg/dL)	127.54 $\pm$ 11.11	119.9 $\pm$ 8.96	4.83 to 10.45	<0.0001
VLDL Cholesterol (mg/dL)	30.68 $\pm$ 7.48	25.91 $\pm$ 6.63	2.80 to 6.74	<0.0001
HDL Cholesterol (mg/dL)	42.69 $\pm$ 6.85	43.55 $\pm$ 8.06	-2.95 to 1.23	0.42

The stratification of the levels of dyslipidemia was also made for patients having longer duration of diabetes ≥ 10 years. The study group comprising of patients with duration of diabetes ≥ 10 years ($n=74$) showed significantly higher TC ($p < 0.001$), TG ($p < 0.0001$), LDL-C ($p < 0.0001$), and VLDL cholesterol ($p = 0.02$) compared to similar type of patients in the control group ($n=51$). HDL-C, however, remained statistically non-significant ($p = 0.10$) in this stratified group, as shown in Table-IV.

Table-IV: Comparison of Lipid profiles for patients with duration of diabetes >10 years n=125

Study Outcomes	Study Group of patients > 10 years diabetes duration n=74	Control Group of patients > 10 years diabetes duration n=51	95% CI	p-value
Total cholesterol (mg/dL)	211.35±26.69	194.51±23.88	7.623 to 26.06	<0.001
Triglycerides (mg/dL)	178.72±31.43	143.24±18.43	25.78 to 45.18	<0.001
LDL Cholesterol (mg/dL)	127.01±11.38	118.33±10.52	4.70 to 12.66	<0.001
VLDL Cholesterol (mg/dL)	30.46±7.5	27.55±5.99	0.42 to 5.41	0.02
HDL Cholesterol (mg/dL)	41.01±5.8	43.02±8.19	-4.44 to 0.42	0.10

Discussion:

The results of our study showed that dyslipidemia was significantly more common in the study group than controls (78% vs. 53%, $p < 0.001$). Elevated TC, LDL-C, and TG were also higher (all $p < 0.0001$). Low HDL-C was more frequent but not statistically significant ($p = 0.09$). The study group had significantly higher mean levels of TC ($p < 0.0001$), TG ($p < 0.0001$), LDL-C ($p < 0.0001$), and VLDL-C ($p < 0.0001$), while HDL-C showed no significant difference ($p = 0.42$).

Studies conducted previously on this topic have also elaborated that dyslipidemia becomes more significant in diabetic patients with nephropathy making it an important modifiable risk factor.

Kolhar U studied the association between lipid profile and DN in T 2 DM. The results shared an incidence of dyslipidemia by 90% in patients with DN and this was significant among both the genders. The study also mentioned that the patients with poor glycemic control were at higher risk of developing dyslipidemia. This association of DN was significant for TC, TG and LDL-C however, no association was established with HDL-C.¹⁴ *These findings are aligned with our results, where nephropathy exhibited significantly elevated LDL and TG but no significant impact on HDL.* Palazhy S and Viswanathan V studied the degree

of dyslipidemia in Type 2 diabetic patients who had developed nephropathy. A similar group of diabetic patients without nephropathy was taken as control group. The incidence of dyslipidemia in patients with DN was reported as 75.28% while it was reported 56.52% in the control group ($P = 0.012$). The major parameters including TC, TG and LDL-C were significantly high in study group compared to control group. However, no significant difference was noted in the levels of HDL-C.¹³

Behera S studied the presence of dyslipidemia in Type 2 DM with DN and made a comparison with lipid profile of Type 2 DM without DN in eastern parts of India and showed significantly raised levels of TC, TG, and LDL-C in type 2 DM with DN.¹⁵ *Similarly, Kumar S and Kishore K further supported our observations, demonstrating that dyslipidemia worsens with the progression of nephropathy, particularly in older diabetics. In that cross-sectional study on dyslipidemia in Type 2 DM with DN, in comparison to Type 2 DM without DN, DN abnormally accelerated the lipoprotein metabolism and reported dyslipidemia 73.3% of the patients with DN compared to 46.7% without DN ($p = 0.03$). All the parameters of lipid profile including TC, TG, LDL-C and HDL-C were significantly affected in patients with DN (p -values = 0.003, 0.004, 0.001 and 0.001 respectively).¹⁶ The cross-sectional study by Hassan H et al. showed increased levels of TG ($p < 0.001$) and LDL-C ($p < 0.001$) in patients having proteinuria compared to patients with normoalbuminuria.¹⁷*

Raina UM in a recent study conducted in Pakistan recorded the frequency of dyslipidemia in patients with and without micro albuminuria. The comparison between the 2 groups regarding dyslipidemia showed that hypertriglyceridemia was present in 91.8% of the cases with DN while in 57.13% cases without DN ($p = 0.000$). The levels of LDL-C were significantly raised in patients with DN compared to without DN (84.19% Vs 59.95%, p -value = 0.017). There was however no statistically significant difference regarding decrease in HDL-C levels among the 2 groups.¹⁸

The studies discussed above especially conducted in South Asian region parallel our results, suggesting regional consistency in dyslipidemia patterns among nephropathy patients, possibly due to shared genetic or socioeconomic risk factors.

Most of these studies including our study showed no statistically significant difference in case of HDL-C. This lack of significant HDL variation, suggests that nephropathy primarily impacts atherogenic lipids (LDL, TG) rather than protective HDL, warranting targeted lipid-lowering strategies. In summary, the results of our study further reinforce the recommendations that lipid lowering agents should go hand-in-hand with lifestyle changes, proper advice and patient's education.

The major limitations of our study include the single-center design and cross-sectional nature. Future larger multicenter cohorts will be helpful for further validation of these findings.

Conclusion:

Diabetic patients with nephropathy displayed a markedly higher and severe degree of dyslipidemia, with raised TC, LDL, TG, and VLDL levels. These findings underscore nephropathy as an independent atherogenic lipid abnormality in type 2 diabetes. Early identification and aggressive management of dyslipidemia therefore be prioritized in diabetic patients, especially once nephropathy emerges, to mitigate future CV and renal complications.

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No

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