

FREQUENCY OF DYSLIPIDEMIA IN TYPE 2 DIABETICS WITH OVERT NEPHROPATHY

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ABSTRACT

Background: Diabetes mellitus a major public health problem has shown a rising trend in the few decades. Globally, 463 million people suffer from diabetes. In Pakistan, the number is alarmingly high. Diabetic nephropathy is chief microvascular complication seen in 46% patients with type 1 diabetes, 20% in type 2 diabetes and overall prevalence of 21%. DN is leading cause of ESRD around the globe.

Objectives: To study the frequency of dyslipidemia in type 2 diabetics with overt nephropathy.

Methods: This was a descriptive cross sectional study, conducted on 146 patients of diabetes mellitus in department of Medicine of Pakistan Railways Hospital, Rawalpindi from 1st May 2024 to 31st October 2024. The sample included the patients of diabetes with overt nephropathy between 30 to 60 years of age. Demographic and biochemical data along with duration of diabetes and duration of nephropathy were entered on structured proforma. Dyslipidemia was considered positive if serum triglyceride >150mg/dl, total cholesterol >200mg/dl, LDL cholesterol >130mg/dl, and HDL cholesterol < 35mg/dl. SPSS version 24.0 was used for data analysis.

Results: This study has shown that dyslipidemia was present overall in 50.68% patients while raised LDL-C being most prevalent lipid abnormality present in 58.9% patients. Hyper triglyceridemia was present in 53.4% and low HDL-C in 31.6%. Dyslipidemia was significantly higher in females 67.6% vs. 32.4% in males.

Conclusion: Our study concluded that overt diabetic nephropathy is associated with higher frequency of dyslipidemia.

Key words: diabetes, diabetic nephropathy, dyslipidemia, cardiovascular disease

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INTRODUCTION

Diabetes mellitus a major public health problem has shown a rising trend in the few decades. Globally, 463 million people suffer from diabetes. In Pakistan, the number is alarmingly high. Around 26.7% of adults in Pakistan were diagnosed diabetics in the year of 2022 according to International Diabetes Federation.^{1,2} Diabetic nephropathy is chief microvascular complication seen in 46% patients with type 1 diabetes, 20% in type 2 diabetes and overall prevalence of 21%. DN is leading cause of ESRD around the globe.^{3,4}

The development of DN involves multiple metabolic, haemodynamic and inflammatory factors and complex interactions. Long standing hyperglycemia leads to mesangial expansion possibly due to glycation of mesangial proteins. Extracellular matrix build up thickens glomerular basement membrane. Oxidative stress and inflammation damage podocytes together with increased intra glomerular pressure leads to proteinuria. Proteinuria is linked with increased cardiovascular events as well as it enhances progression of chronic kidney disease.^{5, 6, 7}

Patient with overt nephropathy develop systemic hypertension which has deleterious effects on microvasculature and hemodynamics. Hypertension in diabetics adversely affects renal disease. Isolated systolic hypertension at home correlates with diabetic nephropathy especially in those less than 65 years of age.⁸ Concomitant obesity and metabolic syndrome enhance the risk of diabetic nephropathy by causing systemic hypertension, glomerular hyperfiltration and renal vasodilatation. Longer duration of diabetes with persistent hyperglycemia potentiates risk of diabetic nephropathy.⁹

Diabetic nephropathy worsens dyslipidemia in diabetics by reducing activity of lipoprotein lipase, lipoprotein clearance and size of LDL particles, thus elevate triglyceride, LDL-C and reduce HDL-C. Abnormal lipid profile potentiates progression of diabetic nephropathy by causing endothelial dysfunction, lipid deposition and atherosclerosis. Lipid peroxidation, inflammation and tissue damage intensify decline in renal function. Diabetes-related dyslipidemia is characterized by high total cholesterol (82.1%), increase in triglyceride levels (73.7%) and high low-density lipoprotein cholesterol (LDL-C) (94.2%) but a decrease in high density lipoprotein cholesterol (HDL-C) (46.9%).^{10,11} A study done in south east Nigeria has shown 66.7% patients of overt nephropathy due to diabetes had dyslipidemia.¹² Dyslipidemia is responsible for 2% increased morbidity and approximately 4.5% of the total mortality worldwide.¹³

Although studies were done in Pakistan to see the association of lipid abnormalities with diabetes mellitus but the studies on dyslipidemia in overt diabetic nephropathy are few. Therefore, we conducted a study to assess the frequency of dyslipidemia in patients with overt diabetic nephropathy in our local population. Early recognition of dyslipidemia and diabetic nephropathy and aggressive management by life style modification and drug therapy greatly reduce morbidity, mortality and economic burden of disease. As dyslipidemia is a crucial in prevention and management of diabetic nephropathy. Aim of the study is to find frequency of dyslipidemia in patients with overt diabetic nephropathy.

METHODS

This study was done at Pakistan Railways Hospital, Rawalpindi from 1st May 2024 to 31st October 2024. It was descriptive cross sectional study involving 146 patients with diabetic nephropathy. Patients of both genders with type 2 diabetes were enrolled by non-probability consecutive sampling between the age of 30-60 years from medical indoor and OPD after informed consent. After through history and physical examination body weight, height measured and BMI calculated. Urine samples were sent for proteinuria and urine albumin and creatinine ratio. Blood samples were sent for serum glucose, blood urea, serum creatinine, fasting lipid profile. Patients with haematuria, urinary tract infection, ESRD, coronary artery disease were excluded. All data was entered on structured proforma. Diabetic nephropathy was defined as having a proteinuria of >300mg/dl per 24 hours or equitant albumin to creatinine ratio of >2.5 mg/mmol in male or 3.5 mg/mmol in female.¹³ Dyslipidemia was defined if serum total cholesterol was >200mg/dl, serum Triglyceride>150 mg/dl, LDL-C > 100mg/dl, HDL-C < 35 mg/dl.⁹ Sample size was calculated using WHO calculator with confidence level of 95% and absolute precision of 7%. Mean and standard deviations were calculated for age, weight, height, duration of diabetes and diabetic nephropathy. For categorical variables frequency and percentages were calculated using SPSS version 24. Dyslipidemia were stratified with age, gender, BMI, duration of diabetes and overt nephropathy. Chi square test was used after stratification and P value of <0.05 was taken as significant.

RESULTS

Out of 146 patients with diabetic nephropathy, 46 (31.5%) were males and 100 (68.5%) were females and mean age of study participants was 63.41±1.0806 years. The mean duration of diabetes was 10.36 ± 6.30 years. The mean duration of overt nephropathy was 3.32 ± 1.619 years.

Table 1. Clinical profile and biochemical estimations of patients in the study population

Sr. No	Variables	Mean ± SD
1	Body Mass Index	25.93±3.40
2	Fasting Blood Glucose mg/dl	215.35±73.26
3	Total Cholesterol mg/dl	188.99±119.55
4	Triglycerides mg/dl	187.41±63.115
5	LDL-C mg/dl	144.56±49.151
6	HDL-C mg/dl	40.85±8.091
7	Serum Urea mg/dl	55.27±37.31
8	Serum Creatinine mg/dl	1.46±1.05

Sixty five (44.5%) patients had positive family history for diabetes while family history of diabetic kidney disease was present in 8(5.4%) patients. Dyslipidemia was present in 74(50.68%) patients. Hypertension was found in 100(68.5%) patients and 62 (42.5%) were taking ACE inhibitors or angiotensin receptor blocker. 84 (57.5%) patients were taking oral anti-diabetic drugs, 24 (16.4%) were taking oral anti-diabetics drugs and insulin, and 38 (26%) patients were taking insulin alone. 70 (47.5%) patients were taking statins.

Table 2. Frequencies of dyslipidemia and different types of cholesterol in type 2 diabetics with overt nephropathy

Sr No	Variables	n=146 (%)
1	Dyslipidemia	
	Present	74(50.68%)
2	Total Cholesterol	68 (46.6%)
3	Triglycerides	78 (53.4%)
4	LDL-C	86 (58.9%)
5	HDL-C	46 (31.5%)

Table 3. Correlation of Dyslipidemia with Clinical and biochemical features

Variables	Categories	Dyslipidemia n=146		P value (<0.05)
		Yes n=74	No n=72	
Age in years	30-40	6 (8.1%)	2(2.8%)	<0.05
	41-50	2 (2.7%)	6(8.3%)	
	51-60	28 (37.8%)	10(13.9%)	
	61-70	18 (24.3%)	28(38.9%)	
	>70	20 (27%)	26(36.1%)	
Gender	Males	24(32.4%)	28(38.9%)	<0.05
	Females	50(67.6%)	44(61.1%)	
BMI (kg/m ²)	<18.5	2(2.7%)	6(8.3%)	< 0.05
	18.5-24.9	22(29.7%)	44(61.1%)	
	25-29.9	40(54.05%)	18(25%)	
	>30	10(13.5%)	4(5.6%)	
Diabetes duration (years)	1-5	20(27.8%)	30(40.5%)	<0.05
	6-10	14(19.4%)	18(24.3%)	
	11-15	26(36.1%)	8(10.8%)	
	16-20	8(11.1%)	14(18.9%)	
	21-25	4(5.6%)	4(5.4%)	
Overt Nephropathy in years	<1	10(13.5%)	20(27.8%)	<0.05
	1-2	13(17.56%)	44(61.1%)	
	3-4	23(31.08%)	8(11.1%)	
	5-6	28(37.83%)	0	

DISCUSSION

With each passing year, the prevalence of DN is steadily increasing. Dyslipidemia is a significant factor implicated in the evolution of cardiovascular disease and progression of renal injury.⁹ Worldwide rising rates of diabetes are observed in both males and females but varying in rate of complications. Presence of gender

difference in development of diabetic nephropathy is still inconclusive. Males have higher risk for diabetic nephropathy compared to males without diabetes. This risk was not observed in females.⁹ In study done by Fan et al reported women exhibited higher risk for diabetic nephropathy and accelerated decline in renal function over 5 years follow up period.¹⁴ This gender difference may be due to genetic, hormonal factors, time of diagnosis, compliance and response to treatment.¹⁵ Similarly in our study 67.6% of females exhibited dyslipidemia compared with 32.4 % males.

Studies have found that the most important predictor for all forms of nephropathy was the duration of diabetes. Dyslipidemia was found the most when duration of diabetes was between 11 to 15 years (36.1%). In our patients mean diabetes duration was 10.36± 6.30% years. The mean duration of overt nephropathy was 3.32 ± 1.619 years. A study by kelemework et al. revealed that 3.2 times increased risk of developing dyslipidemia in diabetes with duration of more than ten years.¹⁶ Around 15.3% diabetics' patients will develop diabetic nephropathy in 10 years.¹⁷

In our study, hypertension was found in 100(68.5%) patients. Hypertension is linked with a six fold increased risk of diabetic nephropathy than those without hypertension. Hypertension enhances insulin resistance causing dysglycemia and dyslipidemia. Dyslipidemia has been reported in 79.5% hypertensive patients with diabetic nephropathy.¹⁸ Combination of hypertension and dyslipidemia aggravate diabetic nephropathy. Aggressive blood pressure reduction and management of proteinuria have proven to be the most effective means of slowing the progression of both renal and cardiovascular diseases.¹⁵

In our study, dyslipidemia was present in 50.68% of the patients. Palazhy S et al. has done a similar study and he has found 75.28% had dyslipidemia in overt nephropathy patients.¹⁹ We analyzed the subtypes of dyslipidemia, with elevated LDL-C observed in 58.9% of patients, elevated triglycerides in 53.4%, and high total cholesterol in 46.6%. We have found Low HDL cholesterol in only 31.5% patients which is contrary to other studies (73.17%)⁹. This difference might be due to statin therapy as 70 (47.5%) patients were taking statins in our study. Studies have shown that statin therapy provided consistent benefits across all age groups.¹⁸ Mazhar et al from Pakistan reported higher prevalence of dyslipidemia in DN with anemia.²⁰ A study conducted in diabetic patients has shown that dyslipidemia was present in 89.83% patients with BMI more than 30mg/kg².²¹ we observed higher prevalence of dyslipidemia in patients with obesity.

Altered metabolism of lipids is significantly high in patients with DN. It has also been found that

dyslipidemia occurs as a result of kidney dysfunction and dyslipidemia promotes further deterioration suggesting bidirectional relationship.²²

Management of dyslipidemia is important in diabetes as it worsens DN and accelerates the risk of cardiovascular events and death.^{7, 22} Life style modifications with healthy diet, exercise, and weight reduction are vital to reduce insulin resistance. Restoring insulin sensitivity will improve dysglycemia, dyslipidemia, hypertension and visceral obesity. This together with lipid lowering drugs and reduction of proteinuria could be an effective strategy to reduce these complications.

We suggest a few limitations in this study. It is a cross-sectional study representing diabetic patients. It did not analyze the effect of lipid lowering agents with dyslipidemia which had a significant impact on results. Second, we have not studied the impact of differences in lifestyle, caloric intake and diet on lipid abnormalities. So further studies are therefore required and the results cannot be generalized to entire population of diabetic patients.

CONCLUSION

Overt diabetic nephropathy is associated with higher frequency of dyslipidemia.

ETHICAL APPROVAL

Ethical approval of article was granted by the Institutional Review Committee of Islamic International Medical College vide reference No. Appl. # Riphah /IRC/ 23/3127 dated 18 December, 2023.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

HP: Conceived idea, design study, data collection

KF: Manuscript writing, data analysis & interpretation

SK: Manuscript writing, critical revision

RB: Data collection , critical revision

AZ: Manuscript writing , statistical analysis

MF: Review of manuscript, supervision

All Authors: Approval of the final version of the manuscript to be published

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