Original research article

A Research Comparing The Lipid Profiles Of Those With Type 2 Diabetes Without Complications Versus Those With The Condition Having Nephropathy

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ABSTRACT

Introduction: One of the most serious complications of diabetes is diabetic nephropathy, which is also known to increase the risk of cardiovascular events. Patients with diabetic nephropathy have abnormal lipid levels, which raises their risk of cardiovascular problems. In this study, type 2 diabetes mellitus (T2DM) patients with and without nephropathy had their levels of dyslipidemia compared, and the causes of nephropathy were examined.

Method: Patients with T2DM who had overt nephropathy were included in the study group and those without nephropathy were included in the control group in this retrospective analysis. Age and diabetes duration were matched between the two groups. The case sheets were used to gather information on total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), urea, and creatinine. Equations were used to compute the TG/HDL-C ratio, a proxy for small, dense LDL particles (sdLDL), and the estimated glomerular filtration rate (eGFR). The variables linked to eGFR were identified using multivariate analysis.

Result: 56.51% of control individuals and 75.28% of nephropathy subjects both had dyslipidemia (P=0.011). In comparison to controls, people with nephropathy had a higher percentage of subjects with atherogenic dyslipidemia (high TG+low HDL-C+sdLDL) at 14.60 than controls did at 14.12. Despite there being no discernible differences in serum creatinine, patients with nephropathy had significantly lower mean eGFR values (P=0.001). Multivariate analysis revealed that TC (P=0.007) and HDL-C (P=0.05) were linked to eGFR among the participants in our study.

Conclusion: According to our findings, dyslipidemia was very common in nephropathy patients. Regular testing for dyslipidemia may help diabetic nephropathy patients reduce their risk of adverse outcomes.

Keywords: Cardiovascular risk; Diabetic nephropathy; Dyslipidemia; Small, dense low density lipoprotein

Introduction

A major clinical condition identified in people with diabetes mellitus is dyslipidemia. High plasma triglyceride (TG) concentration, low HDL-C concentration, and increased concentration of small, dense, low density lipoprotein (sdLDL) particles are the defining characteristics of diabetic dyslipidemia. Increased TG synthesis results from the mobilisation of free fatty acids from adipose tissue to the liver as a result of insulin resistance. Long-term

diabetes would cause lipoprotein lipase dysfunction, which would further raise TG levels and lead to the accumulation of big, TG-rich very low density lipoprotein particles, which in turn produce sdLDL particles [1]. Therefore, type 2 diabetes mellitus (T2DM) patients still have a majority of atherogenic sdLDL particles even when their LDL-C levels are not increased [2]. One of the most serious side effects of diabetes is diabetic nephropathy, which is characterised by proteinuria and renal insufficiency. It is a recognised risk factor for both mortality and cardiovascular events [3]. Individuals with diabetic nephropathy are known to have abnormalities in their lipoproteins, and the majority of these patients pass away from cardiovascular causes before their renal failure progresses to end stage renal disease [4,5]. Both quantitative and compositional alterations in lipids are brought on by diabetic nephropathy. Even in diabetic nephropathy patients with normal levels of total cholesterol (TC) and TG, atherogenic sdLDL particle presence is elevated [4].

Dyslipidemia has also been demonstrated to hasten the rate of kidney injury. Dyslipidemia in diabetes patients causes a progressive decrease of renal function, according to clinical and experimental research [6]. It has been suggested that lipids may harm the vascular, mesangial, and tubular cells of the kidneys, albeit the exact mechanism underlying this activity is still unclear [7]. The kidney damage brought on by dyslipidemia in diabetic patients is accelerated further by underlying dysglycemia [8]. Thus, dyslipidemia and nephropathy exacerbate the clinical condition and raise the risk of renal or cardiovascular complications in diabetes patients by working in concert.]

Studies on lipid abnormalities in patients with chronic renal failure have been conducted in India [9,10], however there aren't many of these studies specifically on diabetic nephropathy. We compared the degree of dyslipidemia among diabetic nephropathy patients in a retrospective analysis and assessed the risk factors for nephropathy among them.

METHODS:

Patients

After receiving the required ethical permission, this retrospective investigation was carried out at Patna Medical College, Patna, Bihar. For the study, case files of randomly chosen participants with diagnosed T2DM were reviewed. The study excluded participants with end-stage renal disease, thyroid dysfunction, known coronary artery disease, hematuria, or urinary tract infection. Additionally, participants who performed blood tests at other laboratories or had irregular follow-up or missing data were not included in the study. Subjects without nephropathy were placed in the control group (group 1) after a review of the case sheets, and those with overt nephropathy were placed in the study group (group 2). The following were the admission and exclusion criteria: Subjects in Group 1 had T2DM but no history of albuminuria or proteinuria, as shown by a spot urine sample with 30 mg of albumin per gramme of creatinine in the three most recent lab reports. Subjects in group 2 had overt nephropathy. In this investigation, subjects were judged to have overt nephropathy if they had persistent proteinuria, which was defined as an albumin/creatinine ratio of >300 mg of albumin per gramme of creatinine on a spot urine sample, in at least two of the three most recent urine analyses. For the patients in this group, the beginning of diabetes should have come before the onset of nephropathy. After screening 439 case sheets, we ultimately added 90 people to the control group (group 1) and 80 to the group with diabetic nephropathy (group 2). Age and diabetes duration were matched between the two groups. The case sheets were used to record

anthropometric information such as height, weight, and body mass index (BMI). We also gathered information on their food, lifestyle, and medications.

Laboratory evaluation

Utilizing kits on a BS-400 Mindray Chemistry analyzer, the following substances were analysed in serum: TC, TG, HDL-C, LDL-C, urea, and creatinine. High-Performance Liquid Chromatography was used on a Bio-Rad D-10 system with Bio-Rad kits to measure HbA1c. These analytical techniques had been codified and applied often in the hospital's clinical laboratory. As a substitute indicator for the presence of sdLDL, the TG/HDL-C ratio was determined. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, traceable to isotope dilution mass spectrometry, was used to determine the estimated glomerular filtration rate (eGFR) from the serum creatinine levels for the study participants.

Statistic evaluation

SPSS version 16.0 was used to analyse the data. The quantifiable variables were expressed as mean standard deviation, and the categorical variables as percentages. A P value of 0.05 was regarded as statistically significant when comparing categorical variables using the chi-square test and continuous variables between the two groups using the t-test. Mann-Whitney For continuous variables with large standard deviations, the U test was used, and P 0.05 was regarded as statistically significant in this context as well.To determine the relationship between lipid markers and indications of renal function, Pearson correlation analysis was used. To determine the variables that were each independently linked with eGFR, multiple regression analysis was used.

RESULTS:

For controls and nephropathy subjects, the mean age was 54.27 ± 9.25 years, and the mean duration of diabetes was 10.75 ± 7.60 years, and 12.26 ± 7.03 years, respectively. For these groups, the male to female ratios were 70:21 and 61:27, respectively. A positive family history of diabetes among first degree relatives was present in about 51% of the study participants. Compared to group one, which included 5.42% of the individuals, group two had an 8.98% positive family history of renal disease. 6.51% of participants in group 1 and 12.35% of subjects in group 2 had family histories of kidney illness that could not be determined from case sheets. When compared to controls, nephropathy patients had a greater prevalence of neuropathy, a diabetes-related consequence (P=0.04). However, there was no statistically significant difference in the prevalence of hypertension or retinopathy between the two groups (P=0.498 and P=0.184, respectively).

Of the entire study participants, 67.95% were taking oral hypoglycemic medications, 23% were receiving an insulin and oral hypoglycemic medication combination, and 8.83% were receiving only insulin. The percentage of participants taking oral hypoglycemic medications, oral hypoglycemic medications with insulin, or insulin alone was not statistically different between the two groups when compared (P=0.587, P=0.536, and P=0.388, respectively). In total, 42.53% of study participants were taking statins alone, 4.41% were using statins along with fibrates, and 0.54% were taking statins along with ezetimibe. When the two groups were compared, it was discovered that people with nephropathy had a considerably greater percentage of statin users (31.51% vs. 53.92% P=0.0002).

Between the non-nephropathy and nephropathy groups, there was no discernible difference in the percentage of subjects taking angiotensin converting enzyme inhibitors (ACEi) or

angiotensin II receptor blockers (ARB) (ACEi: 42.39% vs. 41.56%, P=1.1; ARB: 6.51% vs. 12.35%, P=0.490). Between the two groups, there was no discernible difference in BMI (P=0.14). TG, LDL-C, and TC were all noticeably higher in the group with diabetic nephropathy (P=0.002, 0.014, and 0.001, respectively). Subjects with nephropathy had increased serum urea (P=0.066). Despite there being no discernible differences in serum creatinine, patients with nephropathy had significantly lower mean eGFR values (P=0.001).
In the non-nephropathy group, there were 56.51% of participants with one or more forms of dyslipidemia (TC 100 mg/dL, TG 250 mg/dL, HDL-C 25 mg/dL [for males] and 30 mg/dL [for women], or LDL-C 200 mg/dL, or a combination of these disorders), compared to 75.27% of subjects in the nephropathy group (P= 14.12% of participants in the control group and 14.60% of those with nephropathy had atherogenic dyslipidemia.

In this study, atherosclerotic dyslipidemia is defined as TG 150 mg/dL+HDL-C 25 mg/dL for males and 30 mg/dL for women+TG/HDL-C ratio 2. Both the non-nephropathy group (70.32%) and the nephropathy group (75.27%) had higher TG/HDL-C ratios (2), which are employed as substitute markers for sdLDL (**Table 1).**

Table 1: Comparison of the occurrence of dyslipidemia between subjects with and without nephropathy

Variable	**Group 1 Diabetic subjects without nephropathy**	**Group 2 Diabetic subjects with nephropathy**	**P value**
Dyslipidemia	61 (56.51%)	66 (74.27%)	0.011
sdLDL	64 (70.32)	66 (74.27%)	0.771
Atherogenic dyslipidemia	12 (14.12%)	12 (13.60%)	2.0

In the nephropathy group, the proportion of patients having dyslipidemia was lower in statin users compared to non-users (38.45% vs. 64.85%, P=0.013). On the other hand, in the control group, there was no discernible difference in the proportion of participants with dyslipidemia between the statin and non-statin subgroups (32.34% vs. 36.20%, P=0.58). When participants receiving ACEi or ARB were contrasted with those receiving neither (53.32% vs. 48.93%, P=0.672 for controls; 62.4% vs. 58.53%, P=0.702 for the nephropathy group), dyslipidemia was not found to be different.

It was discovered that TC, TG, LDL-C, and sdLDL had a weakly positive association with serum urea (r=0.275, r=0.240, r=0.247, and r=0.325, respectively) and serum creatinine (r=0.286, r=0.238, r=0.25, and r=0.225, respectively), as well as a weakly negative connection with eGFR (r=-0.28, r The established nephropathy indicator eGFR was used as the dependent variable in a multiple regression analysis, with the independent factors being TC, TG, HDL-C, LDLC, BMI, duration of diabetes, and HbA1c. The dependent variable, eGFR, was chosen because certain patients may exhibit "non-proteinuric diabetic nephropathy." It was discovered that among the study participants, TC (P=0.006) and HDL-C (P=0.05) were related to eGFR (**Table 2**).

Table 2:

Independent variable	**Unstandardized coefficient B**	**Standard error**	**P value**	**R square for the model**
BMI	-0.665	0.701	0.342	0.130
Diabetes duration	-0.454	0.352	0.201	-

HbA1c	1.097	1.122	0.331	-
Total cholesterol	-0.231	0.083	0.006	-
Triglycerides	0.001	0.030	0.992	-
HDL-C	0.420	0.224	0.062	-
LDL-C	0.052	0.091	0.552	-

DISCUSSION:

Adults with recently discovered kidney disease should be checked for dyslipidemia, as this condition, while not always present, is frequently present among those with nephropathy, according to Kidney Disease: Improving Global Outcomes (KDIGO) clinical practise guidelines for lipid management in chronic kidney disease [11]. In this study, the nephropathy group had a considerably larger number of individuals with dyslipidemia. While advanced renal impairment also results in a decrease in HDL-C levels, proteinuria, the defining feature of diabetic nephropathy, increases LDL-C fraction [12]. The Diabetes Control and Complications Trial (DCCT) and other large-scale trials' post-hoc analyses have shown that albuminuria is linked to higher levels of TC, TG, and LDL-C [13].

According to the findings of our study, patients with nephropathy had considerably higher levels of TC, TG, and LDL-C. TC, TG, HDL-C, and LDL-C were significantly different between diabetic and diabetic nephropathy patients, according to a study among a comparable South Indian population [14]. Similar findings to those of the present investigation have been found in a study conducted even in a population of a different ethnicity [15]. A different study found that type 1 patients can also have dyslipidemia linked with diabetic nephropathy, not just T2DM people [16]. The mean HbA1c% of the participants in our study (9.531.85 and 9.32.3 for controls and nephropathy cases, respectively) underlines their poor glycemic condition. Since persistent hyperglycemia has a significant impact on lipid metabolism, the dyslipidemia of the study's participants may also be a result of their poor glycemic control.

In this study population, both groups had high rates of participants with sdLDL, as evidenced by the TG/HDL-C ratio, albeit there was no statistically significant difference between the two groups. However, a study of Japanese diabetic people revealed that nephropathy patients' LDL particle sizes were considerably lower than those of subjects without nephropathy [17]. About 13% of participants in both groups had atherogenic dyslipidemia, which is the coexistence of high TG, low HDL-C, and the presence of sdLDL particles. Their likelihood of experiencing unfavourable cardiac events may rise if they have atherogenic dyslipidemia or sdLDL particles. The current study's connection between lipid measures and kidney function parameters suggests that dyslipidemia and renal insufficiency are common in this population. Numerous prospective studies have demonstrated a strong association between dyslipidemia and renal prognosis [18]. The incidence of unfavourable cardiovascular events among people with renal disease has been shown to decrease with therapeutic intervention with statins to lower cholesterol levels [19]. The use of statins to treat dyslipidemia can enhance renal outcomes, according to existing data, albeit this has not been definitively demonstrated [11]. Although statin therapy patients in the nephropathy group in the current study had a decreased incidence of dyslipidemia compared to non-statin participants, the presence of dyslipidemia even among statin users in both groups is alarming.

In this investigation, it was found that the lipid parameters TC and HDL-C were linked to nephritis. Previous research has demonstrated that patients with chronic renal failure who had greater TC levels had a higher probability of dying [20,21]. In a more recent large-scale study

with 3,303 patients with chronic kidney disease stages 3 to 5, Chen et al. [22] found that the relationship between TC and mortality varied depending on the patient's amount of proteinuria. Despite the fact that the HDL-C and eGFR did not significantly correlate according to Pearson correlation analysis, HDL-C was found to be related to falling eGFR in our study based on regression analysis. After accounting for a number of variables, a community-based cross-sectional study found that HDL-C is independently correlated with eGFR in the general population [23]. The Physicians Health Study had shown that, even at mildly raised serum creatinine values, patients with elevated cholesterol or low HDL-C were at considerable risk for worsening renal function [24]. It should be emphasised that the present study's regression analysis results may have been influenced by the small number of patients, uncorrected clinical data, and retrospective study design.

The findings of this study demonstrate that nephropathy patients had poor glycemic and lipid control as well as a significant prevalence of concomitant conditions like hypertension and neuropathy. This justifies thorough therapeutic intervention and early detection of these disorders for the best possible control. Even though it was a retrospective analysis with a limited sample size, the study was nonetheless able to gather important information about the prevalence of dyslipidemia among people with diabetic nephropathy. Although there is no disputing the efficacy of therapeutic interventions like statin therapy in the control of blood cholesterol, prospective trials are required to definitively demonstrate their impact in lowering cardiovascular event-related mortality among nephropathy patients.

Conclusion:

According to the findings of our study, dyslipidemia was much more common in nephropathy patients than in other diabetic participants in this community. Furthermore, the population's risk for future cardiovascular events is increased by the abundance of sdLDL particles found there. It is generally agreed that strict management of dyslipidemia and dysglycemia could be a useful tactic for lowering the risk of renal or cardiovascular problems.

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