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Original Research Article

Examining the relationship between chronic kidney disease, dyslipidaemia, and dysglycemia: a prospective study

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ABSTRACT

Background: Chronic kidney disease (CKD) results in profound lipid disorders, which stem largely from dysregulation of high-density lipoproteins (HDL) and triglyceride-rich lipoprotein metabolism. Objectives were to evaluate the correlation between chronic kidney disease, dyslipidaemia and dysglycemia.
Methods: In-patient and outpatient department (OPD) of department of medicine, COM and JNM Hospital, Kalyani. Cases are defined as patients (>20 years of age) with a diagnosis of CKD (non-oedematous). The controls are defined as age and gender-matched patients (>20 years) attending medicine OPD/indoor without diagnosis of CKD.
Results: Among the CKD cases, 30 individuals were diagnosed as overtly diabetic, whereas in the control group, 22 participants had fasting blood sugar (FBS) levels equal to or exceeding 126 mg/dl. The mean FBS was 111 mg/dl (standard deviation (SD) 44 mg/dl) in the CKD group and 91 mg/dl (SD 31 mg/dl) in the control group. The difference in FBS levels between the CKD patients' group and the control group was statistically significant (p value=0.001).
Conclusions: Hyperglycaemia is also significantly associated with CKD in form of increased fasting blood sugar (47% among cases as compared to 30% in control) and increased post-prandial blood sugar (49% in cases as compared to 36% in controls). Dyslipidaemia occurs in CKD cases (39% among CKD cases and in 24% of controls) in the form of increased triglycerides (TG), LDL and low HDL.

Keywords: Chronic kidney disease, Dyslipidemia, Dysglycemia

INTRODUCTION

Chronic kidney disease (CKD) significantly contributes to morbidity and mortality from cardiovascular disease (CVD) worldwide and is increasingly recognized as an independent risk factor for developing CVD.[1] The relationship between CKD and CVD is complex, with interventions targeting one condition often improving outcomes for the other. In particular, addressing risk factors commonly associated with CKD progression, such as hypertension, diabetes mellitus (DM), and dyslipidemia, has been shown to benefit cardiovascular health.[2]

Dyslipidemia and CKD

CKD is associated with significant lipid abnormalities, primarily affecting high-density lipoproteins (HDL) and triglyceride-rich lipoprotein metabolism. Specifically, CKD disrupts the maturation and composition of HDL and impairs the clearance of triglyceride-rich lipoproteins, leading to elevated plasma concentrations.[3] This impairment in HDL maturation is primarily due to the down regulation of lecithin-cholesterol-acyltransferase, along with increased plasma cholesteryl ester transfer protein (CETP) activity.[3] Additionally, CKD-induced hypertriglyceridemia and abnormal composition of

lipoproteins result from down regulation of lipoprotein lipase, hepatic lipase, and the very low-density lipoprotein receptor, coupled with upregulation of hepatic acyl-CoA cholesterol acyltransferase (ACAT).[4] Furthermore, CKD exacerbates disturbances in triglyceride-rich lipoprotein metabolism by down regulating apolipoproteins, ApoA-I, ApoA-II, and poC-II. These disruptions increase the risk of atherosclerotic cardiovascular disease and negatively impact renal disease progression and energy metabolism. [4]

While plasma triglyceride levels are often elevated in CKD patients, plasma cholesterol levels typically remain normal or decrease, with occasional increases observed in end-stage renal disease (ESRD). The rise in plasma triglycerides in ESRD is associated with impaired elimination of very low-density lipoproteins (VLDL), leading to the accumulation of atherogenic VLDL remnants (IDL). Conversely, plasma low-density lipoprotein (LDL) levels usually remain normal, and plasma HDL levels are consistently low, with impaired transformation of cholesterol ester-poor HDL-3 into cardio-protective HDL-2. [3-5]

Dysglycemia and CKD

CKD often leads to dysglycemia, characterized by irregular blood sugar levels, including hyperglycemia and hypoglycemia. Nephropathy is a significant cause of morbidity and mortality in diabetes, particularly affecting proteinuric diabetic patients. The prevalence of micro- and macroalbuminuria in both type 1 and type 2 diabetes is around 30% to 35%, with significant variation among different ethnic groups.[6] Diabetic nephropathy typically develops later in type 1 diabetes, while around 3% of newly diagnosed type 2 diabetic patients may exhibit overt nephropathy. The risk of developing diabetic nephropathy diminishes with longer diabetes duration. Microalbuminuria is a strong predictor of diabetic nephropathy onset in type 1 diabetes, with a consistent decline in glomerular filtration rate (GFR) over time. Type 2 diabetic patients with nephropathy experience similar declines in GFR.[6-8] Morphological studies have shown a close relationship between glomerular and tubulointerstitial lesions severity and GFR levels, with early alterations in tubular function correlating with glycemic control.[9]

Objectives

Objective of the study was to evaluate the correlation between chronic kidney disease, dyslipidemia and dysglycemia.

METHODS

Study area

The study was conducted at the in-patient and OPD of department of medicine, COM and JNM Hospital, Kalyani from March 2021 to February 2022.

Study population

Study population included adult patients, aged over 20 years, of both genders, who visit the OPD or are admitted to the department of medicine in Kolkata and neighbouring districts. Cases are individuals over 20-years-old who have been diagnosed with non-oedematous CKD. Controls are defined as patients of similar age and gender who visit the medicine OPD or are admitted to the hospital without a diagnosis of CKD.

Inclusion criteria

Case groups were diagnosed with CKD based on: blood urea and creatinine levels, measurement of creatinine clearance (glomerular filtration rate (GFR) through direct laboratory assessment or utilization of the 4-variable modification of diet in renal disease (MDRD) equation, identification of proteinuria as an early indicator of renal damage, assessed by measuring urinary albumin: creatinine ratio (ACR). This excludes other causes of proteinuria through clinic-pathological monitoring. Microalbuminuria is defined as a urinary albumin-to-creatinine ratio (UACR) ranging from 30 to 300 mg/g or a 24-hour urine albumin excretion of 30 to 300 mg, while overt proteinuria is defined as UACR exceeding 300 mg/g or a 24-hour urine protein excretion exceeding 300 mg, whole abdomen ultrasonography (USG), elevated fasting plasma glucose exceeding 100 mg/dl and postprandial glucose levels exceeding 140 mg/dl, or the use of specific medications and elevated total cholesterol levels exceeding 200 mg/dl, triglyceride levels exceeding 150 mg/dl, LDL levels surpassing 100 mg/dl, and HDL levels below 40 mg/dl in males and below 50 mg/dl in females, or the use of specific medications.

Exclusion criteria

Patients ageing <20 years and oedematous CKD patient were excluded.

Study period

The duration of the study was one year (March 2021 to February 2022).

Statistical tool

Statistical tool used for the study was statistical package for the social sciences (SPSS) software.

RESULTS

The correlation between CKD and dysglycemia

According to the American Diabetes Association guideline, fasting plasma glucose levels ranging from more than 100 mg/dl up to 125 mg/dl are considered as impaired fasting glucose, while levels equal to or greater than 126 mg/dl are diagnosed as diabetes. We conducted a

comparison of fasting blood sugar (FBS) levels between both the case and control groups. Hypoglycaemia (defined as FBS <70 mg/dl) was excluded from both groups. The distribution of FBS levels is presented in Table 2.

Among the CKD cases, 30 individuals were diagnosed as overtly diabetic, whereas in the control group, 22 participants had FBS levels equal to or exceeding 126 mg/dl. The mean FBS was 111 mg/dl (standard deviation (SD) 44 mg/dl) in the CKD group and 91 mg/dl (SD 31 mg/dl) in the control group. The difference in FBS levels between the CKD patients' group and the control group was statistically significant (p value=0.001).

Table 1: Distribution of cases according to age and sex.

Age (years)	Cases		Controls	
	Male	Female	Male	Female
20-30	5	2	5	5
21-40	6	4	5	5
41-50	6	6	5	5
51-60	13	8	10	10
Total	30	20	25	25

Table 2: Distribution of FBS levels.

Fasting blood sugar	Normoglycemic (FBS <100)	Impaired fasting glucose (FBS=100-125)	Diabetic (FBS ≥126)
Case	40	11	30
Control	50	6	21

Table 3: Distribution of PPBS levels.

Post prandial blood sugar	Normoglycemic (PPBS <140)	IGT (PPBS=140-199)	Diabetic (PPBS ≥200)
Case	50	11	31
Control	50	15	20

According to the ADA guideline, postprandial plasma glucose (PPBS) levels ranging from more than 140 mg/dl up to 200 mg/dl are considered indicative of impaired glucose tolerance (IGT), while levels equal to or exceeding 200 mg/dl are classified as overt diabetes. The distribution of PPBS levels is presented in Table 3.

Among the cases, 31 individuals were diagnosed as overtly diabetic, while in the control group, 20 participants had PPBS levels equal to or exceeding 200 mg/dl. Through statistical analysis, we determined that the mean PPBS was 165 mg/dl (with a SD of 51 mg/dl) in the patient group and 143 mg/dl (with a SD of 39 mg/dl) in the control group. Consequently, we observed a statistically significant difference in postprandial blood sugar levels between the case and control groups (p value=0.007).

Table 4: Prevalence of dyslipidemia.

Dyslipidemia	Case	Control
Present	40	21
Absent	60	70

The correlation between CKD and dyslipidemia

In our study, dyslipidaemia was observed in 40 CKD cases and in 21 individuals within the control group. Utilizing Fisher's exact test with a 95% confidence interval of 1.044 to 3.392 and an odds ratio of 1.882, we found a statistically significant p value of 0.0393 (less than 0.05). This indicates that dyslipidaemia was notably more prevalent in the CKD group compared to the control group, as demonstrated in Table 4.

Total cholesterol

In our study, the case group showed a mean total cholesterol (TC) level of 170 mg/dl (SD 40 mg/dl), while the control group had a mean TC of 171 mg/dl (SD 31 mg/dl). Among CKD cases, 26 individuals had TC levels exceeding 200 mg/dl, compared to 24 individuals in the control group. However, the difference in TC levels between the CKD patients' group and the control group was not statistically significant (p=0.53) (non-significant).

Triglyceride

In our study, the case group showed a mean triglyceride (TG) level of 159 mg/dl (SD 51 mg/dl), while the control group had a mean TG of 131 mg/dl (SD 50.55 mg/dl). Among CKD cases, 25 individuals had TG levels exceeding 150 mg/dl, compared to 20 individuals in the control group. We identified a statistically significant difference in TG levels between the case and control groups (p=0.001).

High-density lipoprotein (HDL)

In our study, the case group showed a mean HDL level of 41 mg/dl (SD 9.9 mg/dl), whereas the control group had a

mean HDL of 45 mg/dl (SD 9 mg/dl). Among CKD cases, 32 individuals had low HDL levels according to sex-specific criteria (<40 in males and <50 in females), compared to 21 individuals in the control group. We detected a statistically significant difference in HDL levels between the case and control groups (p=0.0346) (significant).

Low-density lipoprotein (LDL)

In our study, the case group showed a mean LDL level of 111 mg/dl (SD 51 mg/dl), whereas the control group had a mean LDL of 99 mg/dl (SD 39 mg/dl). We identified a statistically significant difference in LDL levels between the CKD case and control groups (p=0.0027) (highly significant). Consequently, we observed a statistically significant presence of dyslipidaemia in CKD patients compared to age- and sex-matched individuals in the control group.

DISCUSSION

India has recognized as "Diabetes capital," with its Asian-Indian populations showing genetic predisposition to early insulin resistance, resulting in a higher incidence of diabetes. The International Diabetes Federation's Diabetes Atlas 2006 predicts that India could have 69.9 million diabetics by 2025 unless preventive measures are taken. Additionally, Asian-Indian populations exhibit more renal damage and a higher prevalence of metabolic syndrome and diabetes-related organ damage compared to other ethnicities. Asians, in general, demonstrate a heightened susceptibility to renal damage compared to Caucasians. In diabetic patients, inadequate control of blood sugar levels significantly increases the risk of developing nephropathy.[10,11]

Tonelli et al reported a diabetes prevalence of approximately 38.5% among CKD patients, with diabetes being linked to cardiovascular disease across CKD stages 1 through 4, a finding consistent with our study's non-edematous CKD case group.[8]

Our study unveiled a notable difference in lipid profiles between CKD patients and the control group. Dyslipidemia was prevalent in 42 CKD cases (40.38%) versus 27 controls (26.47%) (p=0.0393, odds ratio (OR) =1.882, 95% confidence interval (CI) 1.044–3.392). CKD patients exhibited significantly higher levels of triglycerides (p=0.001), HDL (p=0.0346), and LDL (p=0.0027) compared to controls. However, there was no statistically significant difference in total cholesterol values between the CKD and control populations (p=0.53).

Research by Dautin et al has highlighted that in CKD, total cholesterol and LDL cholesterol levels typically remain within the high-normal range or even low.[12] Hypertriglyceridemia is the primary dyslipidemic disturbance observed, especially in early CKD stages and in up to 70% of ESRD patients. While hemodialysis tends to improve triglyceridemia, this effect is more pronounced in nondiabetic patients. Reduced activity of lecithin cholesterol acyltransferase contributes to low levels of HDL cholesterol, exacerbated by microinflammation in uremic patients.[13]

The mild and moderate kidney disease (MMKD) study followed 227 patients with primary kidney disease over 7 years, documenting a progressive decline in HDL cholesterol levels in early stages of kidney disease, accompanied by rising triglycerides and significant decreases in average Lp (a).[14]

Lee et al found a proportional relationship between LDL cholesterol levels and adverse cardiovascular outcomes in CKD patients, with the lowest risk observed in those with LDL-C levels below 70 mg/dl, suggesting the appropriateness of setting a lower LDL-C target for managing cardiovascular risk in this population.[15]

Studies by Palazhy et al and Sujatha et al observed hyperlipidemia in CRF patients, while Mikolasevic et al reported dyslipidemia across various groups including those not requiring dialysis, individuals with nephrotic range proteinuria, ESRD patients, and renal transplant recipients.[16-18] Shah et al demonstrated that elevated serum triglyceride (TG) levels independently predict negative renal outcomes in non-dialysis requiring CKD patients, influenced by factors such as age, estimated glomerular filtration rate (eGFR), and albuminuria.[19]

In conclusion, our study's significant association of dyslipidemia with CKD echoes findings from diverse ethnic populations, underscoring the more atherogenic lipid profile prevalent in the Asian ethnic population.

CONCLUSION

Elevated fasting blood sugar (47% among cases compared to 30% in controls) and increased post-prandial blood sugar (49% in cases compared to 36% in controls) are significantly associated with CKD, indicating hyperglycemia.

Dyslipidemia, characterized by increased triglycerides, LDL, and low HDL, occurs in CKD cases (39% among CKD cases compared to 24% in controls).

Our study reflects prevailing trends in our country, highlighting the emergence of epidemics associated with stressful lifestyles, obesity, diabetes, hypertension, and elevated levels of tumor necrosis factor-alpha in the bloodstream. These common inflammatory cytokines provide insight into the association between CKD and various components of metabolic syndrome.

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