



Research Article

Association of Dyslipidemia in Decreased Glomerular Filtration Rate in Patients with CKD KDIGO ≥ 3

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Abstract

Objective. To determine the association of dyslipidemia with decreased glomerular filtration rate (eGFR) in patients with CKD KDIGO ≥ 3 . **Material and methods.** Observational, analytical, longitudinal, ambispective study; was carried out at the Family Medicine Unit (UMF) No. 55 Zumpango, the sample size was calculated using the mean difference formula, with an expected mean of 5.2, obtaining $n = 90$ patients with CKD KDIGO ≥ 3 , between 20-69 years. Patients with dyslipidemia and without dyslipidemia were classified into 2 groups, in which creatinine was evaluated to calculate the estimated glomerular filtration rate (eGFR), total cholesterol and triglycerides, subjects with renal function replacement therapy, patients with pathologies or treatments that modify lipid metabolism. For the bivariate analysis, the Student's T test and the Mann-Whitney U test were applied according to the type of distribution presented by the eGFR values for the groups with and without dyslipidemia. **Result and conclusion.** Based on the eGFR values for the groups with and without dyslipidemia, they show that patients aged 20 to 69 years with CKD KDIGO ≥ 3 with dyslipidemia presented a mean eGFR of 40.24 for the first analysis, and 34.70 for the follow-up analysis., with a mean difference of 5.53, which was significant ($p = 0.003$).

Keywords: Dyslipidemia; Cholesterol; Triglycerides; Chronic Kidney Disease (CKD); Glomerular Filtration Rate (GFR).

Introduction

Chronic Kidney Disease (CKD) is a progressive and silent disease, CKD is an umbrella term for a group of heterogeneous disorders that affect kidney structure and function, which manifest in various ways depending on the underlying cause and severity of the disease. [1]

The Kidney Disease Improved Global Outcomes (KDIGO) defines CKD as “persistently elevated urine albumin excretion (creatinine ≥ 30 mg/g [3 mg/mmol]), persistently reduced estimated glomerular filtration rate (eGFR < 60 mL/min per 1.73 m²), or both, for over 3 months, with health implications.” [2]

In Mexico, an increase in the prevalence and incidence of CKD has been observed. There is no national registry of kidney patients, therefore, various sources estimate that in our country there are around 129,000 patients with CKD and only about 60,000 receive some type of treatment. Since 2006, Mexico, Chile and Uruguay have increased the incidence rate of CKD from 16% to 38%, and in Argentina, Brazil, Chile and Mexico, the prevalence has increased from 30% to 45%, the latest data obtained in Mexico report that, in 2017 there was a prevalence of CKD of 12.2% and 51.4 deaths per 100 thousand inhabitants in Mexico. [2-7]

The severity of CKD varies, with renal disease with normal function or end-stage renal disease, the latter occurs when the glomerular filtration rate decreases to less than 15 ml/min per 1.72 m², the renal disease is usually of insidious onset and sometimes asymptomatic, until a glomerular filtration rate of less than 30 ml/min per 1.73 m² is present.

According to the KDIGO guidelines, the staging of CKD is based on the estimated GFR (eGFR) in 6 categories: G1 to G5, with G3 subdivision into a and b; and albuminuria in 3 categories A1, A2 and A3.

- According to the eGFR they are: G1 > 90 (Normal or high); G2 60-89 (Mild decrease); G3a 45-59 (Mild-moderate decrease); G3b 30-44 (Moderate to severe decline); G4 15-29 (Severe decline); G5 < 15 (terminal ERC)
- According to albuminuria and albumin/creatinine ratio: A1 < 30 (Normal mild increase); A2 30-300 (Moderate magnification); A3 > 300 (Severe Magnification)

Albuminuria and the albumin-to-creatinine ratio are now considered to be the first laboratory marker for renal structural damage, appearing before any other alteration in eGFR. [8,9]

The etiologies related to CKD can be modifiable and non-modifiable. Smoking, obesity and dyslipidemia are modifiable risk factors, which can be addressed to prevent progression to end-stage CKD, renal function replacement therapies and transplantation. A patient with a history of hypertension is considered to have a five-fold increased risk for the development and progression of CKD, with a pathological history associated with a higher risk. Diabetes mellitus is in second place, it is recognized as a predisposing factor for renal deterioration and during its evolution presents some degree of nephropathy. Finally, in obstructive uropathies, it has been found that they have little association with CKD, however, their presence accelerates the progression of kidney damage, so their monitoring is important for the follow-up of patients.

The non-modifiable ones are the age over 60 years, since in these patients the progression of the disease is slow and mortality is higher. [10-14]

Dyslipidemia in Chronic Kidney Disease

Dyslipidemia is defined as “the alteration in lipid metabolism that produces variations in plasma lipoprotein concentrations.” 3 groups can be identified according to the lipid phenotype: hypercholesterolemia (manifested with an excess of plasma cholesterol concentration [TC]), hypertriglyceridemia (manifested with an excess plasma concentration of triglycerides [TG]), or

mixed dyslipidemia (manifested with an excess of TC and TG). [15]

Dyslipidemia is a progression factor of both CKD and cardiovascular disease, the latter has a risk factor for CKD and vice versa since it causes significant alterations in the lipoprotein profile, defined as the “dyslipidemic profile” of patients with chronic kidney disease; dyslipidemia in CKD is characterized, due to an increase in plasma triglycerides, low plasma HDL-C concentration, normal or slightly elevated LDL-C levels with increases in lipoparticle (Lp) levels, and is associated with increased cardiovascular morbidity and mortality and further deterioration of renal function. [16]

According to its pathophysiology, the mechanisms by which these changes occur are modified as CKD progresses. Theories have been established between the mechanisms underlying atherosclerosis and glomerulosclerosis. [17]

They can be summarized in 4 main aspects: 1. The conversion of lipoproteins into oxidized lipoproteins by mesangial cells and macrophages; 2. Promotion of oxidized LDL from cytokine production; 3. Oxidized LDL stimulation of apoptosis; 4. Macrophage influx and matrix production. [18]

The latest results of dyslipidemia ENSANUT 2018 have a prevalence of 19.5%. It has been observed that patients with CKD tend to have elevated triglyceride. By definition 100% of patients with nephrotic syndrome have dyslipidemia, but in non-nephrotic patients dyslipidemia varies in stages 1 to 4, the prevalence of dyslipidemia varies with the stage of the disease. [19,20] It has been observed that patients with CKD tend to have elevated triglyceride.

In stage 1 to 4 hemodialysis patients, LDL levels are similar to those in the general population, triglycerides and lipoprotein(a) are elevated and HDL is decreased. In peritoneal dialysis, triglycerides and Apo B are elevated by 25-50%, LDL levels are higher in these patients compared to those on hemodialysis. [21,22]

Dyslipidemia is associated with further deterioration of renal function and progression to end-stage renal failure. In any case, evaluation and therapeutic intervention for the control of dyslipidemia in renal patients are mandatory. Dyslipidemia has been linked to the rate of impairment in kidney function, so it is possible that treatment of the alteration in lipid metabolism may contribute to slowing the progression of kidney damage.

Materials and Methods

The main objective of this research was to determine the association of dyslipidemia with the decrease in glomerular filtration rate in patients with KDIGO CKD greater than or equal to 3, therefore an observational, analytical, longitudinal, ambispective

study was carried out that corresponds to a retropective cohort study.

The Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula was used, this formula is measured from the following parameters: creatinine, age, sex, race, and adjustment can be made according to body mass index for a more accurate result, to stage eGFR.

Patients diagnosed with KDIGO V CKD with renal replacement therapy (dialysis, hemodialysis, kidney transplantation) and patients diagnosed with impaired lipid metabolism (primary dyslipidemia, familial hypertriglyceridemia, Gaucher disease, Niemann-Pick disease, Fabry disease, Farber disease, gangliosidosis, Krabbe disease, metachromatic leukodystrophy, Wolman's disease, hypothyroidism, biliary cirrhosis) were excluded.

Patients who did not attend a follow-up for any reason (including death, change of address, no desire to continue participating in the study) at any time were eliminated, as well as patients who did not have laboratory data updated to assess dyslipidemia and eGFR calculation.

This non-probabilistic study of consecutive cases was carried out in the Family Medicine Unit No. 55 in patients aged 20 to 69 years, with chronic kidney disease KDIGO ≥ 3 , forming 2 groups between patients without dyslipidemia and those with dyslipidemia. The sample size was calculated using the mean difference formula with a confidence level of 95%, a statistical power of 80%, with a 1:1 group ratio; with a value of delta 5.2. A sample of 90 subjects was obtained.

Results

In the present research, an initial sample of 90 records of adult patients over 20 years of age with KDIGO >3 chronic kidney disease was carried out at FMU No. 55 Zumpango, of which 17 were eliminated, therefore 73 subjects were included for the statistical analysis.

When analyzing the sociodemographic characteristics of the present study, it was observed that the distribution of the subjects by sex is; 33 (45.2%) for females, 40 (54.8%) for males; The median age was 68 years (IQR 56-75).

According to the pathological personal history, it is reported that 63 (86.3%) had a history of arterial hypertension, 65 (89%) had a history of type 2 diabetes mellitus, 6 (6.7%) had a history of smoking. A mean of 27.19 (± 5.2) was found in relation to BMI, and nutritional status was reported with 3 (4.1%) subjects of low weight, 14 (19.2%) of normal weight, 36 (49.3%) of overweight and 20 (27.4) of obesity.

In relation to paraclinics, the mean cholesterol (mg/dL) was 182.15 (± 42.91), the median triglycerides (mg/dL) were 188 (IQR 120-281), and the median creatinine (mg/dL) was 1.6 (IQR 1.4-2.1).

Taking the creatinine result, the eGFR (ml/min/1.73m²) was calculated, obtaining a median 36 (IQR 30.03-49.49). Each patient was staged according to KDIGO, and 23 (31.5%) were in stage IIIa, 31 (42.5%) in stage IIIb, 18 (24.7) in stage IV, and 1 (1.4%) were in stage V.

According to our maneuver, it was found that 49 (67.1%) of the subjects had dyslipidemia, 24 (32.9) did not have dyslipidemia. (Table 1)

Variable	n=73
Age (years) ^a	68 (56-75)
Sex ^b	
Woman	33 (45.2)
Man	40 (54.8)
History of hypertension ^b	63 (86.3)
History of diabetes ^b	65 (89)
Smoking habit ^b	6 (8.2)
BMI (kg/m ²) ^c	27.19 (± 5.2)
Nutritional status ^b	
-Low weight	3 (4.1)
-Normal weight	14 (19.2)
-Overweight	36 (49.3)
-Obesity	20 (27.4)
Causal diagnosis ^b	
-Diabetes	58 (79.5)
-Hypertension	3 (4.1)
-Other*	12 (16.4)
Biochemical parameters	
-Total cholesterol (mg/dL) ^c	182.151 (± 42.91)
-Triglycerides (mg/dL) ^a	188 (120-281)

-Creatinine (mg/dL) ^a	1.6 (1.4-2.1)
Glomerular filtration rate (ml/min/1.73m ²) ^a	36 (30.03-49.49)
KDIGO Stadium ^b	
-IIIa	23 (31.5)
-IIIb	31 (42.5)
-IV	18 (24.7)
-V	1 (1.4)
Presence of dyslipidemia ^b	49 (67.1)

a. Median and CI ranges; b. frequencies (n) and percentages (%); c. mean and standard deviation *Other: Prostatic hyperplasia, obesity

Table 1: Clinical and demographic characteristics of adults older than 20 years with stage > 3a chronic kidney disease

Analyzing the causal diagnosis of Chronic Kidney Disease, compared by the presence of dyslipidemia, we found T2DM as the most frequent causal diagnosis, 40 (69%) patients living with diabetes and presenting dyslipidemia, while 18 (31%) subjects with diabetes did not present dyslipidemia, followed frequently with dyslipidemia to other conditions with 7 patients (58.3%), while 5 (41.7%) of the subjects with other conditions did not present dyslipidemia and finally 2 subjects with SAH (66.7%) presented dyslipidemia and 1 (33.3%) subject with SAH did not present dyslipidemia, without these differences presenting statistical significance $p=0.775$. (Table 2)

Variable	With dyslipidemia n= 49	No dyslipidemia n= 24	Significance p
Diabetes	40 (69)	18 (31)	
Hypertension	2 (66.7)	1 (33.3)	0.775**
Other*	7 (58.3)	5 (41.7)	

*Other: Prostatic hyperplasia, obesity **X2

Table 2: Causal diagnosis of CKD in adults over 20 years of age with nephropathy grouped by the presence of dyslipidemia.

Dyslipidemia has a prevalence of 67.1% in this population analyzed.

The results obtained based on the eGFR values for the dyslipidemia and non-dyslipidemia groups show that patients aged 20 to 69 years with KDIGO chronic kidney disease greater than or equal to 3 with dyslipidemia had a mean of 40.24 (± 14.44) eGFR for the first study, and 34.70 (± 13.87) for the follow-up analysis.

with a mean difference of 5.53 (± 15.35), in the follow-up of the patients, with $p=0.003$, so the presence of this pathology does lead to a decrease in the glomerular filtration rate. (Table 3)

	Mean (SD)	Mean Difference	p
Initial eGFR	40.2410 (± 14.44)		
Final eGFR	34.7024 (± 13.87)	5.5385 (± 15.35)	0.003*

eGFR is reported in ml/min/1.73m². c. mean and standard deviation *T student for related samples

Table 3: Reduction of glomerular filtration rate in patients with CKD KDIGO >IIIa, contrasting the initial eGFR and final eGFR.

When comparing the presence of dyslipidemia with the stage of renal function of the subjects, no statistically significant difference was observed between the presence of dyslipidemia and renal function at baseline ($p=0.437$). (Table 4)

		ERC STADIUM					
Dislipidemia		Stage 2	Stage 3A	Stage 3B	Stage 4	Stage 5	p
Initial	Absent ^a	0 (0)	8 (33.3)	7 (29.2)	8 (33.3)	1 (4.2)	0.437**
	Present ^a	0 (0)	15 (30.6)	24 (49.0)	10 (20.4)	0 (0)	
Final	Absent ^a	1 (3.8)	6 (23.1)	5 (19.2)	13 (50.0)	1 (3.8)	0.656**
	Present ^a		9 (19.1)	21 (44.7)	10 (21.3)	6 (12.8)	
		1 (2.1)					

a. Frequency and percentage. ** Mann-Whitney U.

Table 4: Initial comparison of the presence of initial and final dyslipidemia in relation to the stage of renal function.

At follow-up, there was no statistically significant difference between subjects with and without dyslipidemia and the stage of renal function at 6 months of follow-up ($p=0.656$), so no association was observed between the presence of dyslipidemia and the stage of renal function in the subjects. It was observed that in subjects the progression of renal failure in subjects with dyslipidemia was greater compared to subjects without dyslipidemia, with a frequency for stage 5 of CKD of OR cases at baseline rising to 6 cases (12.8%) at the second measurement. (Table 4)

Next, the comparison of the initial and follow-up glomerular filtration rate for the presence of dyslipidemia was performed, observing that the filtration rate was higher in the subjects with the presence of dyslipidemia at both times, the initial eGFR in subjects without dyslipidemia was 38.80 ± 13.31 , while the subjects with dyslipidemia presented a mean eGFR of 40.24 ± 14.44 with a difference of 4.43 ml/min/1.73m², The difference was not significant ($p=0.210$), for the final evaluation the mean initial eGFR was 31.24 ± 16.16 and at the end of follow-up it was 31.24 ± 16.16 with a difference of 3.45 ml/min/1.73m², this difference was not significant ($p=0.347$). It was observed that subjects with dyslipidemia presented a decrease in eGFR of 5.54 ml/min/1.73m², while subjects without dyslipidemia presented a decrease of 4.56 ml/min/1.73m², so the decrease in eGFR is greater in subjects with dyslipidemia. (Table 5)

Dyslipidemia		eGFR b	Difference	P
INITIAL	ABSENT	35.80 \pm 13.31	4.43	0.210**
	PRESENT	40.24 \pm 14.44		
FINAL	ABSENT	31.24 \pm 16.16	3.45	0.347**
	PRESENT	34.70 \pm 13.87		

eGFR in (ml/min/1.73m²) b. Mean and Standard Deviation - *Student's T

Table 5: Comparison of glomerular filtration rate by the presence of initial and final dyslipidemia.

According to the results obtained between eGFR and cholesterol, no statistical significance was observed when analyzing the correlation between serum cholesterol levels and eGFR, with a value of $r = -0.108$ ($p = 0.363$). (Figure 1)

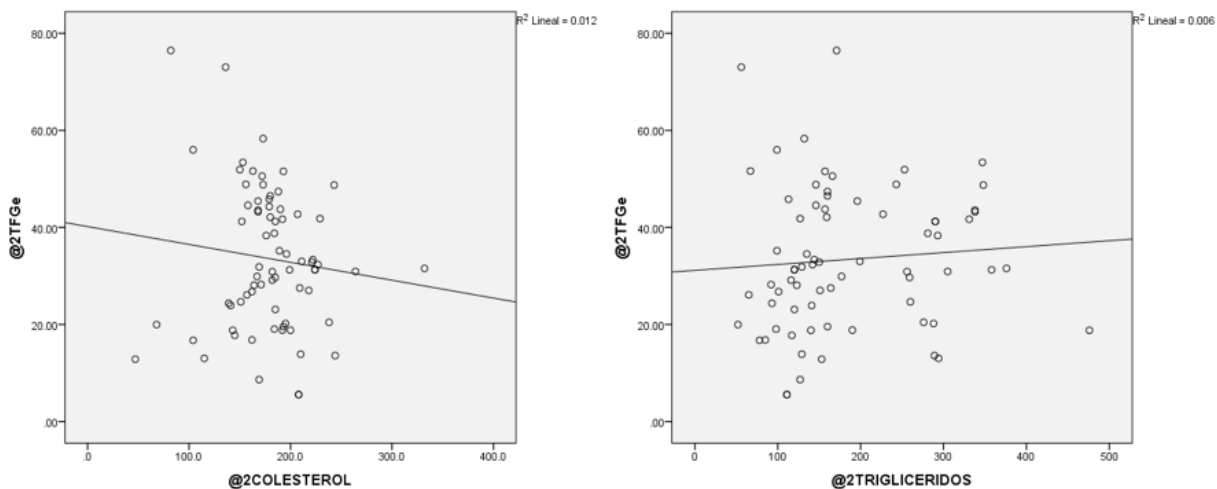


Figure 1: Correlation between total cholesterol, triglycerides, and estimated glomerular filtration rate in patients with chronic kidney disease in KDIGO greater than or equal to 3.

Subsequently, the correlation of serum triglyceride levels with eGFR was analyzed, reporting a difference of 0.192 ($p = 0.107$), so there is no significant correlation in eGFR and serum triglyceride levels.

Discussion and Conclusions

In the present study, the prevalence of dyslipidemia in chronic kidney disease was 67.1%. It was found that patients aged 20 to 69 years with KDIGO ≥ 3 chronic kidney disease with dyslipidemia presented a decrease in eGFR of 5.54 ml/min/1.73m², while subjects without dyslipidemia presented a decrease of 4.56 ml/min/1.73m², so the decrease in eGFR is greater in subjects with dyslipidemia. Regarding the stage of CKD, it was determined that the progression of renal failure in subjects with dyslipidemia was greater compared to subjects without dyslipidemia, with a frequency for stage 5 of CKD from 0 cases at the beginning to 6 cases (12.8%) in the second measurement, so we infer that in subjects with renal failure the progress of this is greater.

This study demonstrates that dyslipidemia is an important factor for the progression of chronic kidney disease, which agrees with the study conducted by Dr. Jorge Armando Poll Pineda et al., in Santiago de Cuba, in a case-control study comparing the presence and/or absence of dyslipidemia in patients with chronic kidney disease. An Odds Ratio (OR) of 3.57 with a confidence interval (CI) of 1.41 – 9.19 with $p < 0.05$ was evidenced, showing that patients with dyslipidemia were more likely to have CKD than those who were not exposed. In another study conducted by Chuan Wang et al., in Shandong, China, decreased eGFR was studied in patients with T2DM with poor triglyceride control, finding that as

long as hypertriglyceridemia was present there was a risk of rapid progression of nephropathy compared to patients with consistently abnormal TG levels, the risks were even higher in patients who experienced a transition from normal TG in the presence of hypertriglyceridemia.

These data indicate the need to support the basis for the design of interventions from the first level of care that allow the evaluation and therapeutic intervention for the control of it, since it has been related to the range of deterioration in renal function, so it is possible that the treatment of the alteration in lipid metabolism contributes to reduce the progression of kidney damage.

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Ethical Considerations

The present study was approved by the Local Health Research Committee 1402, with Institutional registration number R-2022-

1402-018. This is based on the Institutional Ethical Standards, as well as on adherence to the regulations of the General Health Law on Health Research, in force in Mexico. The research carried out is considered category II, with minimal risk.

This research follows the national and international norms cited below: Political Constitution of the United Mexican States, General Health Law, Regulations of the General Health Law on Health Research, Regulations of the Federal Commission for the Protection against Health Risks. Official Mexican standard NOM-012-SSA3-2012, which establishes the criteria for the execution of research projects for health in human beings. Official Mexican standard NOM-004-SSA3-2012 that establishes the criteria for confidentiality of the clinical record. All participants signed the informed consent form after receiving the information about the study as well as the risks and benefits of the study, and were informed about their rights to privacy, confidentiality, anonymity, and protection of personal data. Participants were able to leave the study if they said so at any stage of the study.

Conflict of Interest: No Conflict of Interest

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