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Associated Factors for Chronic Kidney Disease in Patients with Diabetes Mellitus 2: Retrospective Study

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Introduction: Chronic kidney disease affects the quality of life of people with diabetes mellitus, increases cardiovascular risk, and has high social costs.

Objective: To determine associated factors for chronic kidney disease in people with diabetes mellitus type 2.

Material and Methods: Retrospective cohort study with 371 patients evaluated in primary care for diabetes mellitus. Information on age, sex, disease duration, comorbidity and laboratory results was obtained. Patients of both sexes attended between 2022 and 2024 were included. Patients with other renal diseases or referrals were excluded. Logistic regression analysis was performed to identify associated factors.

Results: Males (p = 0.014), age >60 years, (p = 0.01) uncontrolled diabetes (HbA1C >7.99%±1.84) and disease duration over 20 years (p = 0.02) are associated factors for chronic kidney disease (CKD). HbA1c had significant differences between those with and those without CKD. The most frequent comorbidities are arterial hypertension (70%), dyslipidemia (43%), overweight/obesity (44%) and anemia (31%). CKD stage G2 is the most frequent (45%). One hundred percent of patients in G1 and G2 CKD stages have an elevated microalbuminuria/creatinuria rate, and 13% of patients between G3a and G4 stages have this rate within normal values. Most patients receive nephroprotection with ARA II and ACEIs.

Conclusion: It is important to screen for kidney disease in patients with diabetes mellitus type 2 who are male, over 60 years of age, with uncontrolled HbA1c and prolonged disease duration, as well as to treat comorbidities and nephroprotection regardless of the stage of chronic kidney disease.

Keywords: chronic kidney disease, diabetes mellitus type 2, stages of kidney disease

Introduction

Chronic kidney disease (CKD) is a prevalent pathology that affects the quality of life [1] and the physical and mental health[2,3] of individuals, with a high family and institutional cost, especially when it reaches terminal stages. It has been described that up to 40% of patients with diabetes mellitus type 2 (T2D) may have CKD.[1]

Although prevalence figures vary from one country to another, it is estimated that about 10% of Spanish adults may have CKD.[1,4] In the United States, Canada, Europe and Japan, prevalence varies between 8% and 11%.[4] In Peru, the age-adjusted prevalence of CKD was 1.46% between 2014 and 2017 and the highest rate of CKD was in Callao (5.89%) followed by Lima (2.81%). In 2021, 13.07% of Peruvians presented CKD, G1 to G4 and 0.10% of the population was dialyzed,[5] which contrasts with the scarce number of nephrologists and dialysis services.[6]

Type 2 diabetes mellitus (T2D) has a high prevalence and it is estimated that by 2030, 578.4 million people in the world will have T2D, a figure that will rise to 700.2 million by 2045.[7] In Peru for the year 2017, the prevalence of T2D was estimated at 5.6% and prevalence adjusted for age and sex at 5.9%[8] while for the year 2021 diabetic nephropathy was considered as a cause of CKD in 24.77%.[5]

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T2D is considered a heterogeneous disease whose clinical presentation and evolution can vary considerably.[9] It can be diagnosed based on fasting plasma glucose ≥126 mg/dL or at 2 hours (≥200 mg/), during a 75 g oral glucose tolerance test or glycosylated haemoglobin (HbA1c) criteria ≥6.5% or plasma glucose of ≥200 mg/dL in patients with symptoms of hyperglycemia.[9,10.]

T2D can be asymptomatic between 4 and 13 years[11] since hyperglycemia develops gradually[12] or symptomatic: polyuria, polyphagia, polydipsia and weight loss; additionally, blurred vision, weakness, pruritus[13] or complications such as peripheral neuropathy, intermittent claudication or microalbuminuria may occur.[14]

Diabetic renal disease is a microvascular complication that affects approximately 35% of patients with T2D that often progressing to CKD G5 with the need for dialysis or renal transplantation. It presents as two phenotypes: albuminuria and altered glomerular filtration rate.[15] In patients with T2D, mortality rises five times in patients with altered glomerular filtration rate, which when accompanied by microalbuminuria, can increase mortality up to ten times.[16]

CKD is defined by the presence of elevated proteinuria or other alterations of tubular origin or structural damage evidenced in images or by biopsy with three or more months of duration.[17] Proteinuria is determinant for the diagnosis of CKD.[18] It may or may not be accompanied by a decrease in the glomerular filtration rate (GFR) <60 mL/min/1.73 m2.[1,4,6]

The most important modifiable risk factors associated with CKD are proteinuria,[1,19] glomerular hyperfiltration,[1] T2D and HT.[1,18,19] HT is both a cause and a consequence of CKD, and T2D is the most frequent cause of advanced stages of CKD.[1] As a factor of progression, proteinuria conditioned by diabetic nephropathy is the main predictor,[19] and elevated HbA1c levels have been associated with a higher risk of CKD.[1]

There are also potentially modifiable factors, such as obesity, smoking, dyslipidemia and hyperuricemia,[1,4] and non-modifiable risk factors such as age, sex and race.[1,20] With advancing age, glomerular and vascular sclerosis and tubular atrophy occur, causing a decrease in GFR and an increase in proteinuria.[21]

Overweight and obesity have shown an association with CKD[22] due to glomerular hyperfiltration.[1,4] Likewise, in CKD, there is a high prevalence of dyslipidemia that influences the progression of renal damage. Serum uric acid values >7 mg/dL can cause nephrolithiasis and nephropathy. In CKD, hyperuricemia is associated with decreased GFR and a higher risk of cardiovascular morbidity and mortality.[1] Anemia[23] and alterations in mineral metabolism are risk factors inherent to CKD and at the same time are a consequence of renal damage.[1,18]

It has been described that the most frequent stages of CKD are G2 to G4 and that more than 60% correspond to males with a mean age of 61.7 years.[24] When analyzing the pathology reported as etiology of CKD in a Colombian study, it was found that 15.7% of patients had DM and 21.7% had concomitant HT + T2D. According to the stage of CKD, 94.3% of the patients were in G1 to G3 stages and 64.8% of the patients with CKD were women.[25]

In a Mexican study, it was determined that the prevalence and mortality rates for CKD directly associated with T2D have doubled and involve mortality prevalences that mainly affect the female population and shortened life expectancy.[26] A Colombian study found a prevalence of CKD of 26.1% in persons with T2D using the CKD-EPI formula. As for albuminuria stages, 70% of the population was in stage A1 (normoalbuminuria).[27]

At the local level, no studies have been found on the associated factors and clinical characteristics of CKD in persons with T2D, so we consider that this study carried out in an ESSALUD primary care hospital allows us to identify the stages of CKD and its associated factors in the adult population with T2D. Likewise, the results of the research will help to systematize information and adapt treatment protocols in primary care hospitals. The objectives of the research are to analyze the prevalence of CKD and its stages in patients diagnosed with T2D and to analyze the modifiable and non-modifiable associated factors for chronic kidney disease.

Materials and Methods

Study Design, Population and Sample

An applied observational analytical retrospective cohort study was conducted.[28,29] The target population consisted of 371 patients diagnosed with T2D treated between July 2022 and July 2024 in a primary care hospital in the province and district of Trujillo.

The sample had a census character because the information was collected from all patients with T2D who met the following inclusion criteria: patients of both sexes with a diagnosis of T2D, with evaluation of renal function by proteinuria, proteinuria/creatinuria ratio and determination of glomerular filtration rate using the CKD EPI formula,[30] with results of glycemia, HbA1c, haemoglobin (Hb), uric acid and lipid profile and complete records in the medical history. Medical records of patients with glomerulonephritis, renal hypoplasia or monorenal hypoplasia, patients on peritoneal dialysis, hemodialysis or with renal transplantation were excluded because they were attended in a more complex facility.

Data Collection Techniques and Instruments

The documentary analysis technique was used for data collection. The instrument designed by the authors made it possible to collect information on non-modifiable factors: age and sex, clinical factors: blood pressure, glycemia, proteinuria, serum creatinine, microalbuminuria/creatinuria ratio, glomerular filtration rate assessed with the CKD EPI formula, and comorbidities. This information made it possible to identify CKD and its stages in the population studied. The instrument was validated by nephrologists and family physicians and the V of Aiken[31] of 0.94 was obtained.

T2D was considered controlled when Hba1c was <7% and fasting glucose <120 mg/dl;[32] overweight when BMI was 25–29.9 and obesity when BMI was > = 30 in adults under 60 years of age; overweight; BMI 28–31.9 and obesity >32 in older adults;[33] anemia if hemoglobin was <12 g/dL for women and <13 g/dL for men; uric acid within normal limits for men: 4–8.5 mg/dl, and for women: 2.5–7.5 mg/dl[32] and blood pressure was considered controlled when the values were <140/90 mm Hg.[34] CKD was considered when the albuminuria/creatinuria ratio was >30 for women and >20 for men. CKD is classified into 5 stages according to glomerular filtration rate. For G3 to G5 stages, a decrease in GFR <60 mL/min/1.73 m2 in the absence of albuminuria and for G1 and G2 stages proteinuria was required.[19,35] The CKD EPI formula was used for CKD staging.[17,30] For laboratory examinations, the authors obtained the information from the medical records of the patients included in the study. These examinations were performed when the patients attended their check-ups.

The medications that each patient received as treatment for hypertension were recorded, identifying those with nephroprotective properties. Nephroprotection was considered when the patient received treatment with angiotensin-converting enzyme inhibitors (ACE inhibitors) or angiotensin II receptor antagonists (ARA II).[36] Essalud does not have other nephroprotectants such as GLP1RA and SGLT2i in primary care. Medicines used for the treatment of diabetes were also registered.

Procedure

Authorization was obtained for access to information from the clinical histories of patients with T2D treated on an outpatient basis. Selection criteria were applied to organize the information by patient in a database, and then the information was analyzed. All the variables recorded by the responsible physician were considered, and the results were presented considering the STROBE checklist. After the statistical analysis, the scientific article was written.

Statistical Analysis

Descriptive and inferential statistics were used, organizing the data in tables and graphs, measures of central tendency and dispersion to analyze the behavior of the study variables.[29] For the bivariate analysis, statistical tests of association were used, such as Pearson's chi-square test for qualitative variables, and the Mann Whitney *U*-test for quantitative variables. Binary logistic regression was used for multivariate analysis. These data were processed using SPSS version 27 statistical software.[37]

Ethical Considerations

The confidentiality and veracity of the data collected during the study were respected and are faithfully presented. Authorship contributions and transparency in conflicts of interest were reported.[38] The research has the approval opinion of the Ethics Committee of the School of Medicine - UCV (Opinion 085-CEI-EPM-UCV-2024) and the permission of the Research and Ethics Committee - Red Asistencial La Libertad - ESSALUD, to carry out the research by means of

certificate N° 57. The Ethics Committee of the Faculty of Medicine - César Vallejo University and the EsSalud Research Committee (with institutional review committee functions) gave authorisation to conduct the research.

Due to the research design, informed consent was not required. The manuscript complied with the Declaration of Helsinki and the authors declare that the privacy of the participants has been preserved, the data were confidential and anonymous, as befits a retrospective review.

Conflicts of Interest

The authors declare that they have no conflicts of interest in carrying out this research.

Results

Table 1 shows the associated factors for CKD: male sex (0.014), age older than 60 years (p = 0.01), uncontrolled T2D (Hba1C >7.99± 1.84%) and disease duration more than 20 years (p = 0.02).

Table 1 Descriptive Analysis of Modifiable and Non-Modifiable Associated Factors for Chronic Kidney Disease in Patients with Diabetes Mellitus Type 2

Factores		ENFERMEDAD RENAL		Total	Sig.
		No(%)	Si (%)		
Sex	Man Woman	54 (33%) 108(67%)	96(46%) 113(54%)	150(40%) 221(60%)	0.014[(a)]
Glucose	Controlled Not controlled	67(41%) 95(59%)	71(34%) 138(66%)	138(37% 233(63%)	0.14[(a)]
Hb ≥12(mujeres) Hb ≥13(varones) Hb < 12(mujeres) Hb < 13(varones)	No Yes	118(73%) 44(27%)	145(69%) 64(31%)	263(71%) 108(29%)	0.47[(a)]
Smoking	No Yes	153(94%) 9(6%)	201(96%) 8(4%)	354(95%) 17(5%)	0.43[(a)]
Arterial Hypertension	No Yes	51(31%) 111(69%)	62(30%) 147(70%)	113(30%) 258(70%)	0.71[(a)]
Dyslipidemia	No Yes	105(65%) 57(35%)	119(57%) 90(43%)	224(60%) 147(40%)	0.12[(a)]
Nutritional Status	Underweight Normal Overweight-Obesity	10(6%) 74(46%) 78(48%)	17(8%) 101(48%) 91(44%)	27(7%) 175(47%) 169(46%)	0.59[(a)]
hypothyroidism	No Yes	150(93%) 12(7%)	187(89%) 22(11%)	337(91%) 34(9%)	0.3[(a)]
Disease duration	0 to 5 years old 5.1 to 10 years old 10.1 to 15 years old 15.1 to 20 years old Over 20 years old	49(30%) 46(28%) 32(20%) 16(10%) 19(12%)	34(16%) 64(31%) 42(20%) 30(14%) 39(19%)	83(22%) 110(30%) 74(20%) 46(12%) 58(16%)	0.02
Total		162(44%)	209(56%)	371(110%)	
Age(×±sd)		65.20 ± 10.22	68.39 ± 10.59	67 ± 10.54	0.01[(b)]
HbA1c [(c)] (×±sd)		7.42 ± 1.69	7.99 ± 1.84	7.74 ± 1.80	0.00[(b)]

Notes: (a) The Pearson's chi-square test was used. (b) The Mann Whitney *U*-test was used. (c) Glycosylated haemoglobin.

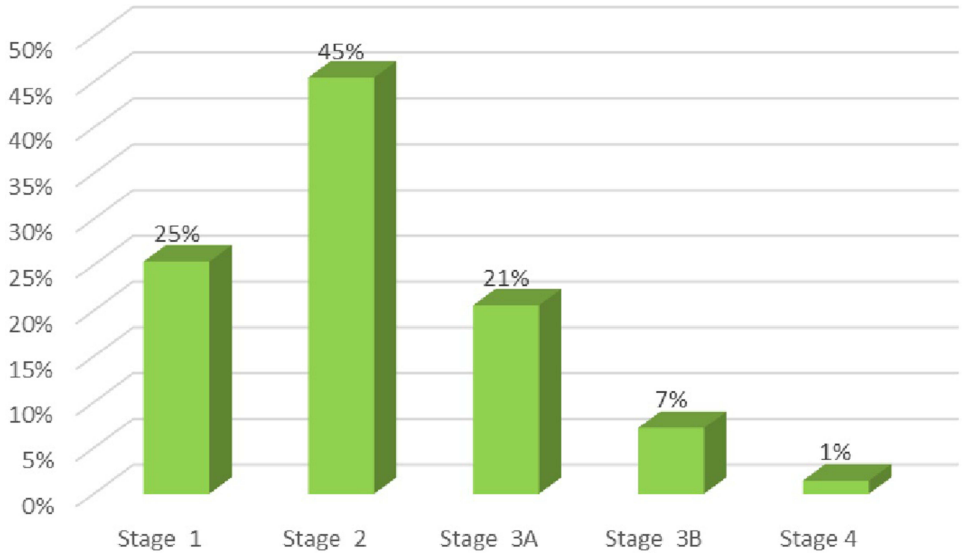

Figure 1 Prevalence of chronic kidney disease according to stages in patients diagnosed with T2D.

Regarding the significance of the test used, sex and disease duration are found to be significantly associated with the presence of CKD; age and HbA1c have significant differences between those with and without CKD.

The most frequent comorbidities are arterial hypertension (70%), dyslipidemia (43%), overweight/obesity (44%) and anemia (31%).

Figure 1 shows that 45% of patients with chronic kidney disease are in G2 stage, followed by G1 stage with 25% and G3 stage with 21%.

Table 2 establishes the binary logistic regression model for modifiable and non-modifiable associated factors for CKD in patients diagnosed with T2D, entering the variables: age, sex and HbA1c. This indicates that there is 1 times greater probability that an older person will have CKD, and there is 2 times greater probability that a male person will also suffer from this disease. Regarding HbA1c, high values are a risk for having CKD. The percentage of prognosis is 63%, which, being greater than 50%, is considered an acceptable model and has been established as follows:

$$P(y) : \frac{1}{1 + e^{-(5.22+0.039X1+0.671X2+0.312X3)}}$$

Where Y: Diagnosis of CKD; X1: Age, X2: Sex (Male) and X3: HbA1C.

To find the logistic regression model presented, the following variables were considered: age, sex, disease duration, glycosylated hemoglobin, smoking, arterial hypertension, dyslipidemia, hypothyroidism, nutritional status, albumin, nephroprotection, uric acid, hemoglobin and number of comorbidities. However, an association was only found with the variables age, sex, and HbA1c.

Table 2 Binary Logistic Regression Model for Associated Factors for Chronic Kidney Disease in Patients Diagnosed with T2D

Factors	B	Standard error	Wald	Sig.	Exp(B)	95% C.I. for Exp(B)	
						Inferior	Superior
Age	0.039	0.015	6.53	0.01	1.039	1.009	1.071
Sex (Male)	0.671	0.298	5.061	0.02	1.955	1.09	3.507
HbA1c	0.312	0.087	12.896	0.00	1.367	1.152	1.621
Constant	−5.22	1.44	13.10	0.00	0.005		

Notes: Summary of the Model: Cox and Snell's R-squared: 0.10 Nagelkerke's R-squared: 0.14. Overall predicted percentage: 63%. SPSS version 27, Wald forward method.

Table 3 Chronic Kidney Disease According to Glomerular Filtration Rate and Microalbuminuria/Creatinuria Rate in Patients with a Diagnosis of T2D

Category by FGe *	Microalbuminuria/creatinuria ratio		Total (%)
	Normal: Men < 20, Women < 30 (%)	Enhanced: Men: ≥20, Women ≥ 30 (%)	
G1 (>90)	0(0)	53(25.4)	53(25.4)
G2 (60–89)	0(0)	95(45.5)	95(45.5)
G3a (45–59)	22(10.5)	21(10)	43(20.6)
G3B (30–44)	5(2.4)	10(4.8)	15(7.2)
G4 (15–29)	1(0.5)	2(1)	3(1.4)
Total	28(13.4)	181(86.6)	209(100)

Note: * (GFR) in mL/min/1.73 m^2.

Table 4 CKD Stages According to Nephroprotection in Patients Diagnosed with T2D

Stages	Nephroprotection		Total	Sig.
	Yes (%)	Not (%)		
Without CKD	128(34.5)	34(9.2)	162(43.7)	0.00
Stage G1	42(11.3)	11(3)	53(14.3)	
Stage G 2	87(23.5)	8(2.2)	95(25.6)	
Stage G 3a	43(11.6)	0(0)	43(11.6)	
Stage G 3b	15(4)	0(0)	15(4)	
Stage G 4	3(0.8)	0(0)	3(0.8)	
Total	318(85.7)	53(14.3)	371(100)	

Note: Kendall's Tau B: - 0.20.

Table 3 shows that 86.6% of patients with CKD have an altered microalbuminuria/creatinuria ratio (M/C). In the analysis by eGFR category, patients in G1 and G2 stages meet both criteria for CKD diagnosis: elevated GFR and M/C. It is also evident that 51% of patients in G3a and one-third of patients in G3b and G4 stages meet the criteria for CKD diagnosis, with the M/C ratio within normal values.

Table 4 shows that, of the patients with chronic kidney disease, G1 and G2 stages, a small percentage of patients do not receive nephroprotection, while in G3a, G3b and G4 stages, all receive it. It is important to highlight that 34.5% of people who do not have CKD receive nephroprotection. Likewise, there is an inverse association between nephroprotection and CKD stage.

Table 5 shows the prevalence of CKD according to stages. In G1 and G2 stages, the majority are women, with high blood pressure, overweight/obesity and an altered albuminuria/creatinuria rate. In stage G3a, the majority are men with high blood pressure and normal BMI. Stage G3b and G4 are mostly women with hypertension, dyslipidaemia, normal BMI and altered albuminuria/creatinuria rate. Most of them receive nephroprotection with ARA II. In stage G3b and 4, the average age is older, longer disease time and anaemia. The albuminuria/creatinuria rate is associated with stage progression, as well as age, disease time and number of comorbidities differ according to stage progression ($p < 0.05$).

Table 6 shows that most patients receive losartan as nephroprotection (59%), followed by enalapril (16%) and then irbesartan (15%).

Discussion

The medical articles reviewed indicate that the prevalence of CKD is higher among males[1,21,39,40] and may be up to three times higher compared to females, with a clearly established relationship between CKD progression and male sex.[21,39] In

Table 5 Prevalence of Associated Factors According to Stages of Chronic Kidney Disease in Patients with T2D

Associated factors		Stage			Total	Sig.
		Stage I, II: eGFR ≥ 60	Stage 3A	Stage 3B Y 4		
Sex	Man Woman	68 (45.9) 80(54.1)	21(48.8) 22(51.2)	7(38.9) 11(61.1)	96(45.9) 113(54.1)	0.78[a]
Smoking	No Yes	143(96.6) 5(3.4)	40(93) 3(7)	18(100) 0(0)	201(96.2) 8(3.8)	0.38[a]
Arterial Hypertension	No Yes	45(30.4) 103(69.6)	11(25.6) 32(74.4)	6(33.3) 12(66.7)	62(29.7) 147(70.3)	0.78[a]
Dyslipidemia	No Yes	83(56.1) 65(43.9)	27(62.8) 16(37.2)	9(50) 9(50)	119(56.9) 90(43.1)	0.61[a]
hypothyroidism	No Yes	133(89.9) 15(10.1)	37(86) 6(14)	17(94.4) 1(5.6)	187(89.5) 22(10.5)	0.6[a]
Nutritional Status	Underweight Normal Overweight-Obesity	12(8.1) 68(45.9) 68(45.9)	4(9.3) 23(53.5) 16(37.2)	1(5.6) 10(55.6) 7(38.9)	17(8.1) 101(48.3) 91(43.5)	0.83[a]
Albuminuria/creatinuria ratio	Normal altered	0(0) 148(100)	22(51.2) 21(48.8)	6(33.3) 12(66.7)	28(13.4) 181(8.6)	0.00[a]
Nephroprotection	Does not have IECA ARA II	19(12.8) 23(15.5) 106(71.6)	0(0) 7(16.3) 36(83.7)	0(0) 3(16.7) 15(83.3)	19(9.1) 33(15.8) 157(75.1)	0.07[a]
Total		148(100)	43(100)	18(100)	209(100)	
Age(×±sd)		65.97± 10.19	73.63± 9.50	75.83+8.41	68.39± 10.59	0.000[b]
Disease duration(×±sd)		2.70± 1.33	3.13± 1.31	3.83± 1.20	2.89± 1.36	0.001[b]
Hb1C[c] (×±sd)		8.17± 1.93	7.598± 1.70	7.358± 1.04	7.985± 1.84	0.131[b]
Hb(×±sd)		13.1± 1.52	12.84± 1.51	12.16± 1.47	12.97± 1.53	0.460[b]
Number of comorbidities(×±sd)		1.36± 0.91	1.42± 0.794	1.33± 0.77	1.37± 0.89	0.047[b]
Uric acid(×±sd)		5.0± 1.39	5.20±1.52	4.94±1.28	4.92± 1.39	0.840[b]

Notes: eGFR: Filtration rate, (a) The Pearson's chi-square test was used. (b) The Kruskal Wallis test was used. (c) Glycosylated haemoglobin.

Table 6 Nephroprotection for Patients Diagnosed with CKD with a Diagnosis of T2D

Nefroprotection	N°	%
Enalapril	52	16
Captopril	2	1
Losartán	188	59
Valsartán	28	9
Irbesartán	48	15
Total	318	100

this regard, it is postulated that kidney function declines more rapidly in men, possibly due to a less healthy lifestyle and the detrimental effects of testosterone.[41] Likewise, mortality is higher among men at all levels of pre-dialysis CKD than among women.[41,42] It has also been described that there are more men on dialysis than women, but the causality of the

differences observed according to sex has not been established with certainty.[42] In the present study, the male sex had CKD in one of its stages (p 0.014) and were twice as likely to have CKD.

Several studies indicate that the variable age over 55 years is also associated with the development of CKD[1,21,25,39,42] and its progression.[15,16,25] The greater number of cases of CKD in older adults is due to the decrease in physiological renal function,[40] secondary to glomerular sclerosis and a decrease in the glomerular filtration rate after 40 years of age, among other factors.[21] In this study, the average age in years was 68.39 and according to the binary logistic regression model applied, there is a greater probability that a person >60 year of age will have CKD.

T2D is a cause of CKD progression,[4,15,16,43] and patients with uncontrolled HT and T2D are at higher risk of CKD progression.[20,25] The binary logistic regression model performed in this research shows that poor metabolic control (HbA1c > 7%) is an associated factor for CKD, which is why, according to the medical literature, monitoring and control of T2D and HT is a key objective to reduce renal deterioration.[20] It has been reported that one-third of patients with T2D may progress to CKD G5[15] and that T2D increases the risk of moderate-to-severe CKD by 4.5 and 6.1 times in men and women, respectively.[15.]

The disease duration with T2D has a direct relationship with the development of CKD, even more so when it is associated with poor metabolic control. In this study, the disease duration referred by the patient was considered, but it should be taken into account that hyperglycemia develops gradually and generally T2D can be asymptomatic or not present the classic symptoms of T2D in early stages. However, there is an underlying risk of developing macrovascular and microvascular complications[11] that lead to the development of CKD.

The most frequent comorbidities in the patients with CKD studied are dyslipidemia, anemia, arterial hypertension, overweight-obesity and hypothyroidism. In the medical literature, we found that dyslipidemia,[1,4,39] anemia,[25,44] and uncontrolled arterial hypertension[1,23,26,27,44] are risk factors for the development and progression of CKD. However, no statistical association was found in this study.

Dyslipidemia is considered a factor in the progression of CKD and is characterized by normal or slightly elevated levels of C-LDL, low C-HDL and high triglycerides due to decreased triglyceride catabolism due to reduced lipoprotein lipase (LPL) and hepatic lipase activity. Changes in lipoprotein profiles are associated with more drastic decreases in GFR, proteinuria, age and the presence of obesity.[45]

In the case of anemia associated with CKD, the main causes are inadequate production of endogenous erythropoietin, decreased erythropoietic response of the bone marrow due to uremic toxins and inflammation, decreased availability of iron for erythropoiesis, shortened red blood cell half-life or deficiencies of vitamin B12 or folic acid[23.] among others. Anemia in CKD can appear from early stages and worsen as CKD progresses. Sometimes it is difficult to differentiate its origin, especially in populations such as the Peruvian population, which has a high prevalence of anemia in the general population and among patients with CKD.[44]

Arterial hypertension is a factor in the development[1,4,35,44] and progression of CKD,[1,18,21,39] especially when it is not controlled, while it is a protective factor when it is controlled.[44] Hypertension acts as a risk factor, a factor initiating renal damage, a factor in the progression of CKD, and a factor that increases morbidity and mortality in CKD.[46,47]

Hypothyroidism in its subclinical[48] and clinical[49] forms is associated with CKD and T2D. Changes in the hypothalamus-pituitary-thyroid neuroendocrine axis are mentioned that seem to be caused by insulin resistance and subsequent compensatory hyperinsulinemia. Insulin has an anabolic effect resulting in an improvement in the availability of TSH and from proinsulin. In addition, C-peptide is released together with insulin from the β-cells of the pancreas. This peptide modulates some cellular functions and promotes the activity of the sodium-potassium ATPase pump required for protein synthesis of many hormones including the HRT.[49] On the other hand, it has been described that patients with CKD have mild reductions in thyroid function, a condition that is accentuated as renal function decreases, and the most common affectation associated with hypothyroidism is the elevation of serum creatinine levels, decreased renal plasma flow and reduced glomerular filtration rate.[48]

The prevalence of CKD in the population studied was 56.33%, with a predominance of G2 (45%), G1 and G3a, and very few cases of G3b and G4, like that reported in the population attended in primary care programs.[20] It is considered that the institutional disposition to attend G1 to G3a stages in primary care hospitals and to refer cases of CKD G3b and

above to a nephrology service in specialized hospitals.[50] Explains the results considering that primary care hospitals are usually centers of first contact and detection of CKD in the population with hypertension and diabetes mellitus type 2.[6]

Among the criteria for diagnosing CKD, proteinuria is a determining factor and may or may not be accompanied by a decrease in GFR.[1,4,17.] About 86.6% of patients with CKD have an altered microalbuminuria/creatinuria ratio (M/C). The patients in G1 and G2 stages meet both criteria for CKD diagnosis: elevated GFR and M/C and a significant group of patients in G3a, G3b and G4 met the criteria for the diagnosis of CKD due to GFR <60 mL/min/1.73 m2 with the M/C ratio at normal values. Therefore, it is important to verify both the M/C rate and the GFR rate for the diagnosis of CKD.

When analysing the comorbidities associated with CKD, it was found that in G1 and G2 stages, as well as G3b and G4 stages, most participants are female, with hypertension and an altered albuminuria/creatinuria ratio. Additionally, in G1 and G2 stages, there is overweight/obesity, whereas in G3b and G4 stages, dyslipidaemia is observed. Some population-based studies report that CKD differs according to gender, with women being more affected than men, especially in G3 CKD.[41]

It is important to mention that, except for age, the other factors are modifiable, such as hypertension and proteinuria[1,18,19] and potentially modifiable, such as obesity and dyslipidaemia.[1,20] Therefore, these factors should be considered as part of the comprehensive approach to patients with T2D and lifestyle changes. It was found that, in G3a stage, the majority are males and have hypertension. The association between male sex, hypertension, and CKD has been described[11,21,40,42,44] It was found that the albuminuria/creatinuria ratio is associated with the progression of the stage of kidney disease, as well as age, disease duration, and the number of comorbidities, which differ significantly according to the progression of CKD stage. These results are consistent with what is described in the medical literature regarding the risk factors associated with CKD.[1,21,40,42] The greater the number of risk factors present, the more advanced the stages of chronic kidney disease.[51]

There is a therapeutic approach to prevent or delay tubulointerstitial atrophy and fibrosis as well as to modify the progression factors of CKD (proteinuria, intraglomerular hypertension and metabolic control in T2D),[1,10] using angiotensin converting enzyme inhibitors (ACEI) and angiotensin II receptor antagonists (ARA II). These drugs reduce albuminuria excretion. ARA II are antihypertensive drugs of choice in patients with CKD and albuminuria with or without diabetes and have demonstrated cardiovascular benefits beyond blood pressure control;[25,36] among them, irbesartan, which decreases the rate of albuminuria in people with T2D, independently of HTN.[36] The population studied received nephroprotection mainly with ARA II followed by ACEI and even a significant number of patients without CKD have this protective factor. Likewise, an inverse association was found between nephroprotection and CKD stage.

We believe that the results regarding hypothyroidism, nutritional status (underweight) and anemia justify further research in the short term, as well as cohort studies to evaluate the effect of nephroprotection and to identify factors of CKD progression in patients with diabetes mellitus. Periodic medical monitoring, education on CKD risk factors, diet, physical activity, and adherence to treatment are required.

Scientific Contribution

This article reports the importance of detecting CKD associated factors in a T2D control program, which should not only assess controlled status but also prevent deleterious effects of CKD on target organs.

Limitations of the Study

A comprehensive assessment of cardiovascular risk and hypoglycaemic medications in the study population was not possible, and as this was a short-term study, a cohort study to assess CKD progression is pending.

Conclusion

Among the non-modifiable associated factors, sex, age and disease duration are significantly associated with the presence of CKD. Among the modifiable associated factors, HbA1c has significant differences between those who have and those who do not have CKD. Hypertension, dyslipidemia, overweight/obesity and anemia and are the most frequent comorbidities in patients with CKD, although no statistical significance was found. Forty-five percent of patients with chronic kidney disease, are in G2 stage, followed by G1 and G3 stages. Most patients with CKD have altered microalbuminuria/

creatinuria ratio and GFRe. Most patients receive nephroprotection with losartan and enalapril. There is an inverse association between nephroprotection and CKD stage.

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Author Contributions

All authors made a significant contribution to the manuscript in the conception, study design, execution, data acquisition, analysis and interpretation. They participated in the drafting, critical revision of the article, gave final approval to the version to be published, and agreed on the journal to which the article was submitted, as well as accountability for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in conducting this research.

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