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ORIGINAL ARTICLE

Chronic kidney disease and progression factors in patients with type 2 diabetes mellitus

Enfermedad renal crónica y factores de progresión en pacientes con diabetes mellitus tipo 2

Doença renal crônica e fatores de progressão em pacientes com diabetes mellitus tipo 2

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ABSTRACT

Introduction: chronic kidney disease is an aggravating condition for the public health system. The detection and timely monitoring of the triggering and progression factors of the disease are a priority in each health system. **Objective:** to characterize chronic kidney disease in patients with type 2 diabetes mellitus with poor metabolic control. **Method:** a descriptive cross-sectional study was carried out on patients with type 2 diabetes mellitus who entered the chronic kidney disease program of the Hospital "Dr. Miguel Enríquez" from October 2021 to January 2023. The population was made up of 175 patients; the sample selected was of 74 patients, who met the inclusion criteria after signing the informed consent. **Results:** there was a predominance of chronic kidney disease in young patients (64% in 18 to 49 years old); likewise; the female sex represented a 65.3%; and duration of type 2 diabetes mellitus of 1 to 5 years in 49.3%. The most frequent comorbidities were dyslipidemia, arterial hypertension and heart failure with a prevalence of 89.3%, 79.3% and 41.3% respectively. The predominant kidney damage stage was grade 2 in a 20.0%; 4% of patients required renal replacement treatment. **Conclusions:** kidney disease usually progresses more in women and in patients with multiple cardiovascular risk factors. Inadequate glycemic control is associated with the progression of kidney disease. Damage to kidney function largely depends on metabolic control.

Keywords: diabetes mellitus; chronic kidney disease; progression

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RESUMEN

Introducción*:* la enfermedad renal crónica es una agravante afección para el sistema de salud pública. La detección y seguimiento oportuno de los factores desencadenantes y de progresión de la enfermedad son una prioridad en cada sistema de salud. **Objetivo*:*** caracterizar la enfermedad renal crónica en pacientes con diabetes mellitus tipo2 con mal control metabólico. **Método*:*** se realizó un estudio descriptivo, de corte transversal en pacientes con diabetes mellitus tipo 2 que ingresaron al programa de enfermedad renal crónica del Hospital Dr. Docente Clínico Quirúrgico Dr. Miguel Enríquez desde octubre 2021 a enero 2023. El universo estuvo compuesto por 175 pacientes, de ellos, se seleccionó la muestra, 74 pacientes que cumplieron con los criterios de inclusión luego de firmar el consentimiento informado. **Resultados:** existió predominio de enfermedad renal crónica en pacientes jóvenes (64 % en 18 a 49 años); así mismo el sexo femenino representó el 65,3 %; y un tiempo de evolución de la diabetes mellitus tipo 2de 1 a 5 años con 49,3 %;las comorbilidades más frecuentes fueron: dislipidemia, hipertensión arterial e insuficiencia cardiaca con una prevalencia de 89,3%; 79,3 % y 41,3 % ; el estadio según el daño renal predominante fue el grado 2 con 20,0 %; el 4 % de los pacientes necesitó tratamiento renal sustitutivo. **Conclusiones*:*** la enfermedad renal suele progresar más en mujeres y en pacientes con múltiples factores de riesgo cardiovasculares. Se asocia a la progresión de la enfermedad renal el inadecuado control glucémico. El daño de la función renal depende en gran medida del control metabólico.

Palabras clave: diabetes mellitus; enfermedad renal crónica; progresión

RESUMO

Introdução: a doença renal crônica é um agravante para o sistema público de saúde.A detecção e monitorização atempada dos factores desencadeantes e de progressão da doença são uma prioridade em cada sistema de saúde. **Objetivo:** caracterizar a doença renal crônica em pacientes com diabetes mellitus tipo 2 com mau controle metabólico. **Método:** foi realizado um estudo descritivo e transversal com pacientes com diabetes mellitus tipo 2 que ingressaram no programa de doença renal crônica do Hospital "Dr. Miguel Enríquez" de outubro de 2021 a janeiro de 2023. O universo foi composto por 175 pacientes, de deles, a amostra foi selecionada, 74 pacientes que atenderam aos critérios de inclusão após assinatura do termo de consentimento livre e esclarecido.**Resultados:** houve predomínio de doença renal crônica em pacientes jovens (64% entre 18 e 49 anos),da mesma forma, o sexo feminino representou 65,3%;e tempo de diabetes mellitus tipo 2 de 1 a 5 anos com 49,3%; as comorbidades mais frequentes foram: dislipidemia, hipertensão arterial e insuficiência cardíaca com prevalência de 89,3%, 79,3% e 41,3% respectivamente. O estágio de acordo com a lesão renal predominante foi grau 2 com 20,0%;4% dos pacientes necessitaram de tratamento de substituição renal. **Conclusões:** a doença renal costuma progredir mais em mulheres e em pacientes com múltiplos fatores de risco cardiovascular.O controle glicêmico inadequado está associado à progressão da doença renal.Os danos à função renal dependem em grande parte do controle metabólico.

Palavras chave: diabetes mellitus;doença renal crônica; progressão

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INTRODUCTION

Diabetes Mellitus (DM) is one of the Noncommunicable Diseases (NCDs) with high prevalence in world population, considered the fastest growing disease in recent years. Statistical data from the World Health Organization (WHO) in 1980 reflect that it was estimated that DM would affect about 108 million inhabitants worldwide; these standards were four times higher in 2014.

According to studies by the WHO and the International Diabetes Federation (IDF) in 2004, they released predictive records that were alarming for the entire health system, example of this, there would be an increase of 150% of the population with DM in the next 25 years, conditioned by the aging of the population; obesity, poor dietary habits and sedentary lifestyle; in one out of every 20 deaths DM will be the cause.[1]

It is stated that 8700 inhabitants per day or 6 inhabitants per minute; and at least one out of ten would be adults between 35 and 64 years of age are diabetic. In the United States of America, the 2017 National Diabetes Statistics Report with 2015 data, originated by the Centres for Disease Control and Prevention, reported 9.4% of the US population with DM.[2]

According to WHO, Chronic Kidney Disease (CKD) affects an estimated 850 million people (more than 10% of the world's population), causes 2.4 million deaths per year, and is currently the 11th leading cause of death globally.[3]

IDF in 2021 the behaviour of DM in adults aged 20-79 years, was 537 million. This is predicted to rise to 643 million by 2030. In addition, there is usually a delay of 4 to 7 years between the onset of the disease and its diagnosis.[4]

CKD is an aggravating and costly disease for the public health system worldwide. The timely detection and follow-up of the disease triggers and progression factors should be a priority in every health system. Establishing protocols and work strategies for the follow-up of the pathology is the guarantee of being able to slow down its progression and prevent its complications.[5]

CKD attributable to DM, or Diabetic Renal Disease (DRD), occurs in 20%-40% of patients with diabetes with 15 years of evolution. In Mexico, DKD is the main cause of renal function replacement therapy in about 50% of patients today in their programs. In recent times, studies have been devoted to define the follow-up and study of the causes that influence the incidence of the disease. Among them are the increase of obesity, both in children and adults, sedentary lifestyle and hypertension, as well as the increase of life expectancy.[6]

In Cuba, CKD has emerged as a problem for the health system. Epidemiological research has shown that the expected prevalence of CKD is 1,800,360 patients, outnumbered by 210,360 patients with chronic renal failure and 3,360 patients with end-stage renal failure. CKD in any of the evolutionary stages is grouped around 3000 patients per million inhabitants each year; in this sense, it has been calculated that approximately 120 of them progress to the final stage of the same and require dialytic treatments to survive or wait for a renal transplant.[7]

The annual statistical report of the Ministry of Public Health of Cuba shows that CKD is the sixth leading cause of death. It is recorded that 850 million people in the world suffer from kidney disease of any etiology (more than 10% of the world's population).[8]

CKD causes at least 2.4 million deaths per year, while acute kidney injury harms more than 13 million people worldwide.[9]

Objective: to describe the factors associated with the progression of Chronic Kidney Disease in diabetic patients with poor metabolic control.

METHOD

A descriptive, prospective cohort study was conducted at the Hospital Docente Clínico Quirúrgico Dr. Miguel Enríquez, in the period October 2021 to January 2023.The study universe consisted of 175 type 2 diabetic patients with poor metabolic control attended at the renal disease consultation of the aforementioned hospital.

Then, among those who met the criteria for inclusion in the study, a sample of 74 patients (n=74) was selected; the size of which was determined according to:

Inclusion criteria: patients of both sexes with biological age equal to or older than 19 years, poor control of DM

Glycemic control: (when meeting criteria): fasting glucose 4.20-6.11 mmol/L; postprandial glucose <10 mmol/L; glycosylated hemoglobin <6.5%.

Blood pressure: ≤130/80 mmHg

Lipids: cholesterol 3.87-5.22 mmol/L; triglycerides 0.68-1.88 mmol/L

Exclusion criteria: pregnant or puerperal patients, patients with chronic kidney disease of other etiology

The following variables were analyzed: age, sex, comorbidity and stages of chronic kidney disease.

Comorbidity (diseases associated with CKD present in the patient). The information was reevaluated by the authors supported by specialists related to the health problem for diagnostic certification: ischemic heart disease, systemic arterial hypertension, cerebrovascular disease, heart failure, obesity, dyslipidemia, peripheral artery disease, chronic kidney disease),

Stages of chronic kidney disease:
Grade 1: Normal or high glomerular filtration rate (>90 mL/min)
Grade 2: Slightly decreased glomerular filtration rate (60-89 mL/min)
Grade 3a: Mildly or moderately decreased glomerular filtration rate (45-59 mL/min)
Grade 3 b: Moderately or severely decreased glomerular filtration rate (30-44 mL/min)
Grade 4: Glomerular filtration rate with severe decrease (15-29 mL/min)
Grade 5: Renal failure (GFR <15 mL/min).

In order to describe the variables under study in relation to the personal pathological history of type 2 DM and the diagnosis of CKD, frequency distribution tables were made in which the results are described in absolute numbers and percentages.

In all cases, informed consent to participate was requested from the patients. The research presented here was carried out under the principles of the Declaration of Helsinki for research in humans. The protocol of this research was approved by the Research Ethics Committee and by the Scientific Council of the Hospital Docente Clínico Quirúrgico Dr Miguel Enríquez, Havana, Cuba.

RESULTS

In the group of patients studied, the mean age was 41 years; only 4.0% of the patients were older than 70 years. Female sex predominated (65.3%). (Table 1)

Table 1 Demographics variables according to progression of chronic kidney disease

Demographics variables	Progression of the CKD		Total	p	RR
	Yes	No			
	n=26 (35,1 %)	n=48 (64,9 %)	n=74 (100,0 %)		
Sex					
Female	20 (76,9)	31 (65,3)	51 (68,9)	0,27	1,8 (0,6 RR 5,4)
Male	6 (23,1)	17 (35,4)	23 (31,1)		
Age (mean ± DE)	44,6 ± 15,0	39,4 ± 12,7	41,2 ± 13,6	0,15	-

Source: survey

Obesity as a risk factor continues to be a factor to be considered, although it did not set the tone in the progression of the disease, with 82.4% of the total patients (Table 2). High systolic arterial hypertension accounted for 57.7% of patients with disease progression.

Table 2 Individual measurements at physical examination according to progression of CKD

Individual measurements on physical examination	Progression of the CKD		Total	p	RR
	Yes	No			
	No. (%)	No. (%)	No. (%)		
Nutritional status					
Normal weight	2 (7,7)	4 (8,3)	6 (8,1)		
Over weight	3 (11,5)	4 (8,3)	7 (9,5)	0,90	-
Obese	21 (80,8)	40 (83,3)	61 (82,4)		
Hemodynamic					
High PAS	15 (57,7)	19 (39,6)	34 (45,9)	0,13	2,1 (0,8 RR 5,5)
High PASd	4 (15,4)	5 (10,4)	9 (12,2)	0,30	-
High PASs	3 (11,5)	7 (14,6)	10 (13,5)	-	-
High PASsd	5 (19,2)	6 (12,5)	11 (14,9)	-	-
PASm	3 (11,5)	1 (2,1)	4 (5,4)	-	-

Table 3 shows that 7 patients maintained uncontrolled glycemia. In 3 of them, glycosylated hemoglobin could not be controlled at one year and, in 2 of them, it worsened in relation to the previous year. All the patients with uncontrolled glycemic control presented progression of chronic kidney disease. Glycemic control and glycosylated hemoglobin control were found to be protective factors against kidney damage (0.2 [0.2 RR 0.4] and 0.3 [0.2 RR 0.4], respectively).

Table 3 DM-related variables according to progression of chronic kidney disease

Variables related to DM	Progression of the CKD		Total	p	RR IC 95 %
	Yes	No			
	No. (%)	No. (%)	No. (%)		
Control	19 (73,1)	48 (100,0)	67 (90,5)	<0,01	0,3 (0,2 RR 0,4)
Hb1c CA	21 (80,8)	48 (100,0)	69 (93,2)	<0,01	0,3 (0,2 RR 0,4)
-TEDM†	7,5±5,7	7,1±6,1	6,8±6,3	0,76	-

CA: control at 2 years; HO+I: oral hypoglycemic agents + insulin;
TEDM: time of evolution of diabetes mellitus in years; †mean ± SD.

Taking into account the comorbidities recorded for each patient, ischemic heart disease was the disease most frequently associated with renal damage, followed by heart failure, the results of which are shown in Table 4. Peripheral vascular disease also had a high presence, which, together with cardiac entities, meant that cardiovascular diseases accounted for 90.5% of the total number of cases.

Tabla 4. Comorbilidad según progresión de la enfermedad renal crónica

Comorbidity	Progression of the CKD		Total	p	RR IC 95%
	Yes	No			
	No. (%)	No. (%)	No. (%)		
Ischemic heart disease	11 (42,3)	21 (43,8)	32 (43,2)	0,90	0,9 (0,3 RR 2,4)
Heart failure	9 (34,6)	11 (22,9)	20 (27,0)	0,27	1,8 (0,6 RR 5,1)
EVP	6 (23,1)	9 (18,8)	15 (20,3)	0,66	1,3 (0,4 RR 4,2)
EPOC	1 (3,8)	3 (6,3)	4 (5,4)	1,00	0,6 (0,1 RR 6,1)
Ulcer disease	1 (3,8)	1 (2,1)	2 (2,7)	1,00	1,9 (0,1 RR 31,3)
Polycystic ER	2 (7,7)	1 (2,1)	3 (4,1)	0,28	4,0 (0,3 RR 45,4)
IC Charlson					
≤ 2 points	19 (73,1)	38 (79,2)	57 (77,0)	0,55	0,7 (0,2 RR 2,2)
≥ 3 points	7 (26,9)	10 (20,8)	17 (23,0)		

COPD, chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; KD, kidney disease; PVD, peripheral vascular disease; CI, comorbidity index.

Only 4% of patients were in need of renal replacement therapy (hemodialysis) at the time of positive diagnosis, so they were not evaluated at progression (Table 5).

Table 5 Variables related to chronic kidney disease according to its progression

Variables related to CKD	Progression of the CKD		Total	p
	Yes	No		
	No. (%)	No. (%)	No. (%)	
Initial stage				
-1	0 (0,0)	10 (20,8)	10 (13,5)	
-2	7 (26,9)	13 (27,1)	20 (27,0)	
-3a	7 (26,9)	8 (16,7)	15 (20,3)	0,09
-3b	8 (30,8)	12 (25,0)	20 (27,0)	
-4	4 (15,4)	5 (10,4)	9 (12,2)	
-TEERC†	5,9±6,3	7,0±6,3	6,8±6,3	0,48

DISCUSSION

As has been well studied and has been reflected in every literature consulted, DM is the main cause of end-stage chronic kidney disease. In a meta-analysis performed in Chinese individuals with type 2 DM, to evaluate the long-term decline in renal function and highlight the progression of diabetic kidney disease; with a total of 1.7 million patients with CKD of multiple etiologies and reached end-stage renal failure, 52% had a 30% change and 16% had a 57% change in GFR over two years.

In another prospective cohort of the same study white patients with type 2 DM, 15.6% experienced a rapid GFR decline, defined as >4% per year over a 10-year follow-up period.[10] The author does not record in the study the race of the patient studied, but it is worth noting that in the study he showed that part of the patients studied had disease regression.

Penno G, et al.[11] showed that cardiovascular risk was worse in tertiles (T), T2 and T3. They were independently related to microalbuminuria and macroalbuminuria. Furthermore, the most striking relationship was in males and in younger individuals and was observed in those without previous cardiovascular disease, although the interaction was significant only for age.

Using clinical markers to evaluate the progression of DRE, Cordero P, et al.[12] demonstrated that reduced renal function can occur in the absence of micro- or macro-albuminuria. Other predictors included sex (male), smoking, hypertension, glycosylated hemoglobin level, dyslipidemia, and sensory neuropathy. The greater use of renin-angiotensin system blockers in groups 3 and 4 reflected disease severity and adequate treatment and argued against the non-use of reno-protective agents in contributing to differences in GFR trajectories.

The study disagreed with the previously discussed study regarding the relationship of sex and disease progression. It should be noted that both studies reflect the use of Angiotensin-Converting Enzyme Inhibitors (ACEI) as nephroprotective agents in the early stages of renal disease.

Hernández F, et al.[13] in their study records, the mean age of the individuals was 57.50 ± 18.49 years, which does not coincide with our study where the sick population was younger. The female sex predominated, coinciding with the data reported by the author in his study. This study coincides with that of the author where there was a sample where overweight patients predominated, with a BMI of 27.07 ± 4.91 kg/m2. Regarding blood pressure, 34 (17.9%) with chronic kidney disease had controlled blood pressure and 23 (31.5%) with chronic kidney disease and uncontrolled blood pressure; with a p = 0.02. This also confirms data of interest for our study where poorly controlled hypertension continues to be a target for end-stage damage in diabetic kidney disease.

When comparing the study with the results obtained by Fuentes GAE and collaborators where he presents the stage of renal disease of the studied patients estimating with respect to the degree of GFR were: stage 1 with 39.5 % (IC 95 %, 34.2-45.6), stage 2 with 38.8 % (IC 95 %, 32.7-44.5). This does not coincide with the study, since the highest percentage of patients with stage 2 and 3a were dispensed, respectively. When analyzing the socio-demographic characteristics and laboratories by presence or absence of chronic kidney disease, the following results were obtained: proteinuria with CKD: 26 (60.5 0 %), with very similar values when comparing both studies.[14]

Progression to end-stage CKD is more frequent in patients with albuminuria. A relationship between elevated serum creatinine and urea levels and a lower glomerular filtration rate is expected. Metabolic control will continue to be the mainstay to prevent progression of renal disease.

The study did not coincide with that published by Arana-Calderón CA and collaborators where the highest percentage of the patients studied was male (51.83%). It was also found that 66.51% were older or equal to 60 years of age, which was not the case in our study.[15]

When reviewing the literature we found a study in CKD patients, the decompensation of hypertension in close relation to the increase in BMI, 54% of patients with renal pathology presented BMI values greater than 25, and 27%, values between 24 and 25 of BMI; being a modifiable risk factor both for the development of chronic kidney disease and for its progression.[16,17]

In addition, BMI <25 has been alluded to as a renal disease preserving factor, possibly because of the relationship between obesity and renal damage due to the accumulation of adipose tissue in the different organs, which causes compression of the kidney, with the consequent increase in intrarenal pressure.[18]

The conduct to be followed for each patient with CKD has been studied and protocolized. Early diagnosis and adequate follow-up of the progression factors are necessary to avoid the adverse effects associated with CKD, including cardiovascular damage, end-stage renal failure and death.[19]

When investigating on anthropometric indicators and their relationship with uncontrolled diabetes in patients with kidney disease there is the finding of identifying the prevalence of 17% of patients with altered urine albumin excretion (12% microalbuminuria and 5% macroalbuminuria), as well as a glomerular filtration rate < 60 mL/min in 6.6% of the population studied. The study identified that altered urine albumin excretion was associated with modifiable risk factors such as waist circumference and fat percentage, as well as higher glycosylated hemoglobin levels.[20]

CONCLUSIONS

Diabetic Kidney Disease tends to progress more in women and in patients with multiple cardiovascular risk factors. Moreover, it is significantly associated with inadequate glycemic control. This indicates that renal function impairment is highly dependent on metabolic control. Control of risk factors, specifically DM, is the most effective strategy to prevent progression of kidney disease.

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