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Original

Chronic kidney disease of nontraditional causes, mortality rates and hospital discharges

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Abstract

Aim: to describe trends in primary diagnosis of death, hospital discharge diagnosis as well as potentially lost years of the life of patients with chronic kidney disease compatible with chronic kidney disease of nontraditional causes, according to data recorded in publicly accessible databases in the country between 2014 and 2019.

Methods: a descriptive longitudinal study was made of the information on deaths and hospital discharges registered in public access databases on the primary diagnosis of chronic kidney disease compatible with chronic kidney disease for non-traditional causes. The results obtained were used to calculate percentages and absolute and relative frequencies of mortality and hospital discharges. General, specific, and adjusted mortality rates were calculated by the direct method. In addition, the years of potential life lost in the country were estimated by province and sex.

Results: in Costa Rica, between 2014 and 2019, 2548 deaths and 1893 hospital discharges related to chronic kidney disease of non-traditional causes. were registered. Adjusted mortality rates were found to be high for the provinces of Guanacaste and Limón compared to national rates and concerning those of other provinces. In the province of Guanacaste, the trend in discharges was also high. In addition, it was detected that the years of potential life lost showed a progressive and constant increase in the country, predominantly in the male sex and in the province of Guanacaste. Thirteen deaths were reported in persons under 20 years of age.

Conclusions: The updating of data on mortality trends has allowed us to identify that the provinces of Guanacaste and Limón have adjusted rates higher than the national average, as well as lower average ages at death compared to the rest of the provinces. Deaths and hospital admissions in persons under 20 years of age suggest early renal damage unrelated to occupational disease. Mortality and years of potential life lost provide information on the burden of disease on the country's population. It should be added that specific coding to monitor the pathology was poorly recorded in the study period.

Keywords: chronic renal failure, epidemiology, mortality records, patient discharge, Costa Rica.

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Abbreviations:
AVPP, Years of life potentially lost
CCSS, Costa Rican Social Security Fund
ICD-10, International Classification of Diseases, tenth revision
CKD, Chronic kidney disease
CKDnt, Chronic kidney disease of nontraditional causes
INEC, National Institute of Statistics and Census

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Chronic kidney disease of uncertain or nontraditional etiology (CKDnt) is a severe form of progressive renal failure, often diagnosed at a very advanced stage due to the absence of early symptoms and requiring renal replacement

therapies to survive.[1] Its etiology is unrelated to diabetes, hypertension, glomerulopathies, or other known causes of kidney disease.[2] The region of the Americas, specifically the Mesoamerican area on its Pacific coast, has experienced up to four times the world the global mortality rate from chronic kidney disease (CKD), and Costa Rica is no exception.[3]

In Costa Rica, it was not until 2005 that the issue began to receive attention when the Nephrology Service of Hospital Mexico carried out its first analysis of (CKDnt). The results obtained in this study show a pattern of epidemic behavior of the disease in the province of Guanacaste, different from what was happening in the rest of the country.[4]

It is difficult to find complete reports for (CKDnt) before the period studied, as it was not until 2019 that the country established the definition of "confirmed case" and "suspected case," as well as mandatory reporting with a specific and temporary code according to the International Classification of Diseases, tenth revision, CIE-10, according to Decree No. 41628-S, published in the Official Gazette of May 13, 2019. However, there are two publications on epidemiological data epidemiologic data on CKD compatible with CKDnt in the country[3, 5] updated up to 2013.

According to national data published in the journal Acta Médica Costarricense by Rivera and Méndez in 2016, between 1990 and 2013, 8382 deaths due to CKD compatible with CKDnt had been registered in Costa Rica.[3] This descriptive study was able to show how information was being registered under CIE-10 for hospital discharges and deaths with a primary diagnosis of CKD compatible with CKDnt: the province of Guanacaste showed a trend of progressive increase in a premature age range, between 30 and 34 years, about 20 years below the national trend. In addition, it was determined that the population was found to be mostly male (4:1 ratio), in agreement with the study by *Wesseling et al*.[5]

To date, no national research is available that updates and integrates publicly available data on the trend of CKD compatible with CKDnt and CKDnt in Costa Rica.[3] For this reason, the objective of this study is to describe the trends of the primary diagnosis at death, the diagnosis at hospital discharge, as well as the years of potential life lost in patients with chronic kidney disease compatible with chronic kidney disease of non-traditional causes according to data registered in publicly available databases in the country between 2014 and 2019.

Methods

A descriptive longitudinal study was conducted based on the information recorded during 2014-2019 in the national public access databases and retrospective information records.

For the study of mortality, we used the databases of deaths provided by the National Institute of Statistics and Census (INEC) and, for the analysis of hospital discharges, the national databases provided by the Costa Rican Social Security Fund (CCSS). On the other hand, for the calculation of the rates, we used the national projections published on the INEC website.

Information on the primary diagnosis of CKD compatible with CKDnt was compiled, for analysis, according to the records of eight CIE-10 codes, namely: N18.0, end-stage renal failure; N18.1, stage 1 chronic renal failure; N18.2, stage 2 chronic kidney disease; N18.3, stage 3 chronic kidney disease; N18.4, stage 4 chronic kidney disease; N18.5, stage 5 chronic kidney disease; N18.8, other chronic renal failures; and N18.9, unspecified chronic kidney failure. Also, at the suggestion of the Pan American Health Organization (PAHO) to include a specific code for the study of non-traditional CKDnt, codes U50 from Chapter XXII of CIE-10 were included (U50.4, CKDnt stage 4; U50.5, CKDnt stage 5 and U50.9, unspecified CKD for CKDnt), as outlined in the Protocol for the Surveillance of Non-traditional Chronic Kidney Disease (Ministry of Health, Directorate of Health Surveillance. San José, Costa Rica: 2019).

The study population was established with the information registered in the publicly accessible national databases of all persons older than 10 years of age, of both sexes, who died or were discharged with a primary diagnosis of CKD compatible with CKDnt and CKDntD in the period between 2014 and 2019. Variables for this study include sociodemographic information (sex, age, place of residence, nationality), registration (discharge centers, place of death, and year), and diagnosis (according to the CIE-10 code) were noted.

The analysis of the data was carried out first using an exploratory approach to the databases with information on deaths and discharges; percentages were calculated as well as absolute and relative frequencies. Then, using the World Health Organization (WHO) standard population[6] and by the direct method, general, specific, and adjusted mortality rates were estimated.

Years of potential life lost (YPLL) is an estimate of how many more years a person would have lived if he or she had not died (specifically from kidney disease in the case in question); this data was estimated for the whole country and according to province and sex. For this study, the age of 65 years was considered the final limit of life, and all deaths occurring in patients between 10 and 64 years of age were included. The choice of the upper age limit is because it is the most commonly used in the regular publications of several countries and is proposed by the World Health Organization (WHO). The formula for calculating it is as follows:[7]

$$\text{AVPP} = \sum_{i=l}^{L}[(L-i)xd_i]$$

Where

I: Lower age limit established (10 years for this study).
L: Upper age limit established (65 years for this study).
i: Age at death
d_i: Number of deaths at the age i.

Life expectancy at birth was not used because it varies according to population, sex, and time of calculation, which represents a limitation for establishing comparisons between the results obtained from different communities over different periods, contrary to what is desirable for a good indicator. The tools used for the analysis were Excel and SPSS version 21.

This study is outside the biomedical research profile protected by the legislation in force and is based on the analysis of information from public access and anonymized databases (patient identification is not allowed), therefore, it does not require the approval of the Inciensa's Scientific Ethics Committee.

Results

Of 161 730 deaths in Costa Rica between 2014 and 2019, 2547 were registered as deaths due to CKD compatible with CKDnt (N18.0-18.9) and 1 due to CKDnt (U50.5), respectively for a total of 1.57% of deaths due to CKD in the CIE-10 categories analyzed. The average age at death was 70.33 years (±17.25) in a range from 10 to 99 years; while 62.2% (n= 1585) of the deaths corresponded to men (other data of the deceased are shown in Table 1).

Regarding the nationality of the deceased, 1585 (62.23%) were Costa Rican and 249 (9.77%) were foreigners, of which 189 were Nicaraguan nationals (7.4%). On the other hand, the provinces with the highest percentage of deaths were San José with 724 (28.4%), and Guanacaste with 538 (21.1%). Seventy-five percent (1912 cases) of deaths were registered in hospitals and 13 deaths were in children under 20 years of age.

Regarding the age at death registered for CKD in the categories under study and mortality, it was found that: the average age was 70.33 years (+17.25), the highest mortality occurred in persons aged 65 years and older, and 34% of deaths occurred in younger persons. Mortality due to CKD according to categories N18.0, N18.5, and N18.9 (of the CIE-10) distributed by age group is shown in Figure 1, where diagnosis N18.9, unspecified chronic renal failure, was the most frequent and with the highest prevalence according to increasing age. In the age range between 10 and 14 years, deaths due to CKD compatible with CKDnt are reported under CIE-10 categories N18.0 and N18.5.

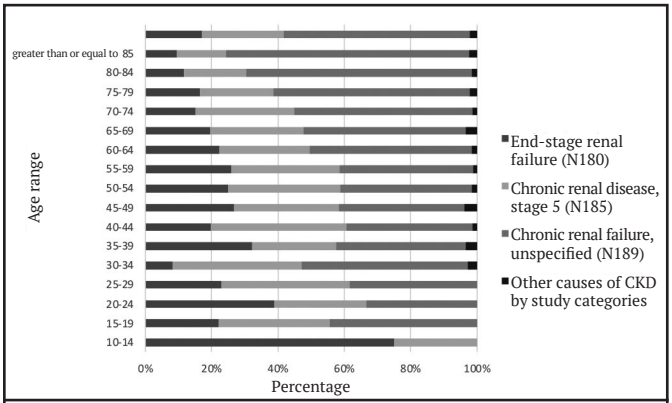

Figure 1. Distribution of mortality by age ranges according to the national registry of people with chronic kidney disease, period 2014-2019, Costa Rica.

For the period 2014-2019, in the country, the adjusted mortality rate showed an increase from 6.92/100 000 to 9.36 /100 000. The province that presented the highest rate was Guanacaste, where in 2014 it was 19.18/100 000, and in 2019 it reached 24.04/100 000. In second place was the province of Limón with rates that varied between 5.27 and 9.73/100 000 during the same period. In these two provinces, the adjusted rates remained steadily high over time, and the lowest average age at death recorded was 65.68 years (+17.35) for Guanacaste and 68.73 years (+17.91) for Limón. Another relevant fact was that the province of Guanacaste reported deaths under categories N18.0 and N18.9 (of the CIE-10) in persons 15 years of age and older (Figure 2).

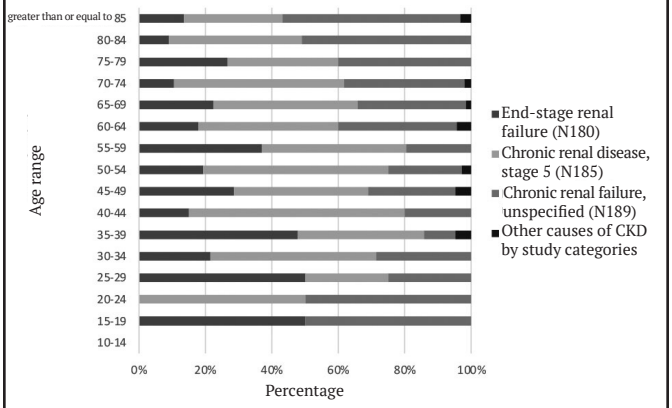

Figure 2. Distribution of mortality by age ranges according to the national registry of people with chronic kidney disease, period 2014-2019, Guanacaste, Costa Rica.

On the other hand, a total of 1893 hospital discharges with diagnoses of CKD N18.0-18.9 (of CIE-10) were recorded in the period 2014-2019. Code U5.0 CKDnt was not recorded in the system at the time.

The average age of the discharged patients was 61.00 years (±3.92) with a range from 10 to 99 years; 68% of the discharges corresponded to men (n= 1,299), with the highest percentage coming from medical centers located in the attraction area of the province of Guanacaste (Table 1).

Table 1. Distribution of deaths and discharges of persons recorded with chronic kidney disease of uncertain or non-traditional etiology (CKDnt) according to age group, province of residence, CIE-10 code, and hospital of discharge, period 2014 -2019, Costa Rica

	Deaths (n=2548)		**Hospital discharges** (n=1893)	
	Frequency	**%**	**Frequency**	**%**
Age groups				
10-14	4	0,2	75	4
15-19	9	0,4	89	5
20-44	210	8,2	552	29
45-64	643	25,2	645	34
65 and over	1682	66,0	475	25
Lost	0	0	57	3
Province of residence				
San Jose	724	28,4	374	20
Alajuela	398	15,6	342	18
Cartago	254	10,0	121	6
Heredia	226	8,9	161	9
Guanacaste	538	21,1	478	25
Puntarenas	191	7,5	228	12
Limon	217	8,5	189	10
CIE-10 classification				
End-stage renal failure (N180)	436	17,1	235	12,4
Stage 1 chronic kidney disease (N181)	0	0,0	4	0,2
Stage 2 chronic kidney disease (N182)	1	0,0	3	0,2

continue

	Frequency	%	Frequency	%
Stage 3 chronic kidney disease (N183)	22	0,9	13	0,7
Stage 4 chronic kidney disease (N184)	29	1,1	6	0,3
Stage 5 chronic kidney disease (N185)	625	24,5	339	17,9
Other chronic renal insufficiencies (N188)	1	0,0	11	0,6
Unspecified chronic renal insufficiency (N189)	1433	56,2	1282	67,7
Chronic kidney disease due to nontraditional causes (CKDnt) (U505)	1	0,0	0	0,0
Hospital centers				
H. Enrique Baltodano Briceño	250	9,8	260	13,7
Hospital Mexico	205	8,0	70	3,7
Hospital Calderón Guardia	264	10,4	221	11,7
Hopital Nacional de Niños	2	0,1	131	6,9
Hospital Tony Facio	72	2,8	124	6,5
Hospital La Anexión	85	3,3	113	6,0
Hospital San Vicente de Paul	107	4,2	81	4,3
Hospital San Juan de Dios	160	6,3	70	3,7
Others	1403	55,1	823	43,5

Source. Prepared by the authors with data obtained from the INEC and CCSS open-access databases.

Regarding the nationality of the hospital discharges, 84.80% were Costa Rican (n= 1606) and 15.20% (287) foreigners.

Finally, an estimated 13,132.5 YPLL due to CKDnt in Costa Rica were estimated for the period 2014-2019, which shows an excess of mortality at relatively low ages; in addition, in the country, a progressive and constant increase in YPLL was observed, predominantly in the male sex and the province of Guanacaste (Table 2).

Table 2. Annual distribution of years of potential life lost (YPLL) due to chronic kidney disease of uncertain or nontraditional etiology (CKDnt) by sex and province, 2014-2019, Costa Rica

Variable/year	2014	2015	2016	2017	2018	2019	Total
YPLL	1945	1474,5	1952,5	1877,5	2327,5	3555	13132,5
In Men	1385	927	1387,5	1372,5	1630	2612,5	8387,5
In Women	560	547	565	505	697,5	942,5	4745,0
Province							
San José	392,5	382,5	417,5	482,5	470	1362,5	3507,5
Alajuela	325	235	272,5	315	357,5	462,5	1967,5
Cartago	117,5	95	140	297,5	257,5	382,5	1290
Heredia	90	55	127,5	97,5	55	187,5	612,5
Guanacaste	550	462,5	675	537,5	765	615	3605
Puntarenas	287,5	135	182,5	60	122,5	187,5	975
Limón	182,5	110	137,5	87,5	300	357,5	1175

Source. Prepared by the authors with data obtained from the INEC databases.

Discussion

The results of this descriptive study show that the primary diagnoses of death and hospital discharge for CKD in the study categories according to CIE-10, document the registration of CKD compatible with CKDnt during the period 2014-2019. The CIE-10 categories under which CKD is compatible with CKDnt being recorded correspond to several codes (N18.0, N18.9, N18.5), as had been identified in 2016.[3] Code U50 (specific for CKDnt) is almost not recorded in deaths and is not used for reporting discharges. There are changes in adjusted mortality rates in the province of Limón that were not reported in previous epidemiological studies.[3, 5] In addition, this study found a progressive and steady increase in YPLL findings reported in the study published in 2016.[3]

During the period 2014-2019, a deficiency in recording persists in identifying CKD patients and their disease stage using administrative codes, despite the administrative code system well described in the literature for this purpose. [8,9] A study by Jalal *et al* in 2019, showed that CIE-10 codes cannot be effectively used to identify CKD patients as the disease stage progresses rapidly.[10]

According to Bello *et al*., in a 2017 study [11], the planning, development, and implementation of nephrology services require reliable databases and information systems to capture information on trends in morbidity-mortality burden, processes of care, and related outcomes. It has been argued that it is very important to detect CKD early enough to be able to implement effective interventions.

Nevertheless, although hospital discharge and death databases are two sources for capturing information as described in numerous studies,[12-15] future pathology surveillance should include an improved model of progression with covariates and highlighting the risk to identify patients who progress rapidly from one stage to another.

The study found that in 2019 only one death was registered with the U50 code for mortality. Therefore, it is considered that the implementation of a specific surveillance protocol for CKDnt implies adaptation and training. If there continues to be an underreporting of deaths in this code, there would be periods of information gaps in which it is necessary to characterize trends in CKDnt for analysis and data are not available.

On the other hand, as already mentioned, the behavior and trend toward increased mortality in the two provinces, Guanacaste and Limón, is striking. Coincidentally, with studies carried out before the time of this study, the province of Guanacaste is described in the literature as a risk zone for CKDnt. [5, 15] On the other hand, the trend in the province of Limón was reported in a study in 2016.[16] The behavior of CKDnt cases in the province of Limón could be explained by the better recording of the disease and awareness of the CKDnt epidemic among health personnel. [17] It should be noted that Guanacaste and Limón also attract the highest proportions of immigrants from other Central American countries, including Nicaragua, where the epidemic of CKDnt has been extensively documented, which may in part explain these findings.[16, 18, 19]

A recent meta-analysis found consistent adverse effects of agrochemicals on the development of chronic kidney disease and, in some cases, association with end-stage renal failure.[1] The adverse effect was also related to cumulative consumption of well water, a possible source of agrochemical exposure.[20] Other studies show that chronic exposure to low concentrations of pesticides produces significant changes in the oxidative stress state, characterized by histopathological changes in the liver and kidneys in animal models.[21-23]

Given the link to the presence of CKDnt in agricultural communities, it is not surprising that pesticides have been suggested as a possible cause of the development of this disease, especially since commonly used pesticides are known as human nephrotoxins.[2] However, evidence has accumulated in the last decade (particularly in the last three years) that poses occupational heat stress as the key cause of the CKD epidemic of the CKDnt epidemic.[15, 24, 25] From a meta-analysis published by Lunyera et al. published by Lunyera et al.[26] it is inferred that the scientific evidence may reflect variation in regional exposures, as well as the difficulties in defining and quantifying agrochemical exposure, but also and quantifying exposure to agrochemicals, but it also highlights the need for epidemiological studies to examine causality, particularly in agricultural communities in agricultural communities in CKD endemic regions.

The YPLL estimates that increase as life expectancy increases and the population ages; however, the increase in YPLL observed here is

not only explained by this situation (increase in life expectancy) but is probably related to a better registration of this disease on death certificates by health personnel and by the personnel who carry out the reassignment process and final coding of the basic cause of death implemented at INEC. In addition, recent studies show that CKDnt is a major contributor to CKD-related premature death and thus to the loss of years of life.[27]

Time-related changes in the YPLL allow prediction of the evolution of premature mortality because they are a more accurate measure than the number of deaths.[28] The changes recorded in the YPLL due to CKDnt during the period 2014-2019 could guide us to what the trends in mortality will be in the coming years.

On the other hand, according to the literature, there are sex-related disparities in the progression of CKD;[29] it has been corroborated that men have a higher risk of death than women. The fact that the male sex is a risk factor for CKDnt could be explained by occupational and environmental exposures such as the triggering effect of high-intensity physical work, heat stress, and dehydration.[30]

Thirteen deaths and hospital discharges in people under twenty years of age suggest the possibility of early kidney damage before occupational exposure, which is consistent with recent studies on the subject. [31-34] Studies in high-risk areas for CDKnt are raising the hypothesis that exposure during childhood may find clinical expression in early adulthood.[34] This hypothesis should be tested in future studies using kidney function tests in children living in at-risk areas, which could lead to early detection and treatment of CKD.

One limitation of this study can be that, since it is founded on databases, there may be potential for underreporting. An attempt was made to minimize this bias by using hospital discharges and mortality databases. Hospital discharges should be interpreted with caution since several could correspond to the same person and the database does not provide the condition of readmission to a medical center for the same pathology.

In conclusion, mortality and YPLL provide information that shows an increasing burden of disease in the population. The update of mortality trends for CDKnt has identified that the provinces of Guanacaste and Limón have higher adjusted mortality rates than the national average and average ages at death lower than the rest of the provinces; in addition, men continue to be more affected by CKD. Deaths and hospital discharges of persons under 20 years of age suggest the possibility of early renal damage before occupational exposure. Finally, CIE-10 specific to monitoring CDKnt was scarcely recorded during the study period. This should motivate the review and improvement of specific registration and surveillance systems for CDKnt, to characterize trends in different geographic locations in specific periods and the timely prevention of the pathology.

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