

# Risk factors associated with chronic kidney disease in adults, an observational study of a single health center in Nicaragua

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## Abstract

**Introduction:** The incidence of chronic kidney disease (CKD) is increasing worldwide due to the aging of the population, early diagnosis, and the increase in its risk factors. The objective of this study was to determine the risk factors associated with CKD in adults from a health center in Santa Teresa -Carazo (Municipality of Nicaragua).

**Methods:** This case-control study was conducted from November 2017 to November 2019. With a probabilistic sample of consecutive sampling for cases and random sampling for controls. The dependent variable (CKD) and the independent sociodemographic variables, family history of CKD, comorbidity, smoking, and use of NSAIDs and PPIs were analyzed. Chi-square (X<sup>2</sup>) and odds ratio was applied, and a significant association was considered if  $P < 0.05$ .

**Results:** 153 participants were included, 51 cases and 102 controls. Risk factors were: age > 60 years (OR 6.65), male sex (OR 4.98), rural origin (OR 1.80), illiteracy (OR 2.46), agricultural occupation (OR 6.73), obesity (OR 2.08), hypertension (OR 8.19), diabetes mellitus (OR 4.85), dyslipidemia (OR 1.23), cardiovascular disease (OR 4.40), and the use of NSAIDs (OR 2.87) and PPIs (OR 4.17).

**Conclusions:** Risk factors for the presence of CKD were components of poverty, such as illiteracy. Possible exposure to nephrotoxins is more common in farmers, so they have a significant risk, as well as patients who chronically take NSAIDs and proton pump inhibitors.

## Keywords:

**MESH:** Essential Hypertension; Proton Pump Inhibitors; Glomerular Filtration Rate; Renal Insufficiency, Chronic; Disease Progression.

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The prevalence and incidence of chronic kidney disease (CKD) are increasing worldwide due to the aging of the population (22 and 40% in those over 64 and 80 years of age, respectively), the increase in its risk factors (cardiovascular disease (CVD), diabetes mellitus (DM), arterial hypertension (HTN and obesity), and the early diagnosis of this disease [1].

In low- and middle-income countries, the prevalence of CKD varies between 14.3% and 36.1%, with an annual incidence of end-stage kidney disease (ESRD) of more than 500,000 patients, constituting a significant health problem, not only because of the requirement of renal support therapy but also because the development of cardiovascular disease (CVD) constitutes the first cause of death in these patients [2].

In Nicaragua, the main reasons for consultation in adults aged 60 years and over are high blood pressure (31%), type 2 diabetes mellitus (28%), and rheumatoid arthritis (15%) (PAHO, 2016) [3]; these data could be explained because nonsteroidal anti-inflammatory drugs (NSAIDs) and proton pump inhibitors (PPIs) are drugs frequently prescribed in health centers; however, their relationship as a risk factor for CKD has not been quantified.

Early detection of CKD risk factors is vital to delay or prevent progression to end-stage renal failure. In Nicaragua, in 2019, according to the Ministry of Health (MINSa), among the most frequent chronic diseases, CKD ranks seventh in incidence and fourth in the population, with a mortality rate of 2.5 per 10,000 inhabitants. In 2019, CKD cases increased almost twice compared to 2017, with an incidence of 21.0 per 10,000 inhabitants (MINSa, 2020) [4].

In the municipality of Santa Teresa, Carazo, according to MINSa, from 2017 to 2019, CKD affected 91 people, with an incidence of 29.4 per 10,000 inhabitants in 2019 (MINSa, 2020). Due to the increasing trend of cases in Nicaragua, there are also no studies available in the SILAIS Carazo and Santa Teresa on risk factors associated with CKD. For this reason, we asked ourselves the following question: What are the risk factors associated with CKD in adults at the Santa Teresa health center from November 2017 to November 2019? Therefore, the objective of the present study was to determine the risk factors for CKD, taking into account traditional factors and other nontraditional factors, such as smoking, profession, illiteracy, and the use of PPIs.

## Materials and methods

### Study design

The present study is observational and analytical of cases and controls.

### Scenery

The study was carried out in the Santa Teresa Health Center outpatient clinic, Silais-Carazo, Nicaragua, from November 1, 2017, to November 30, 2019.

### Participants

Patients older than or equal to 30 years were included. Two groups were formed. The group of cases consisted of patients who presented, for at least three months, a glomerular filtration rate lower than 60 mL/min/1.73 m<sup>2</sup>. The control group consisted of patients treated at the Santa Teresa health center for causes other than CKD during the study period.

### Variables

The variables were age, sex, origin, education, occupation, body mass index, history of CKD, glomerular filtration rate, presence of arterial hypertension, diabetes mellitus, dyslipidemia, cardiovascular disease, smoking, use of NSAIDs, and use of PPIs.

### Data sources/measurements

The source was indirect; the institutional electronic file was reviewed. Laboratory results were obtained from the electronic laboratory record. eGFR was calculated (CKD-EPI) using serum creatinine.

### Biases

To avoid possible interviewer, information, and memory biases, the data were guarded at all times by the principal investigator with a guide and records approved in the research protocol. Observation and selection bias was avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the period above were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

### Studio size

The sample was probabilistic, estimated at 50 cases with a 2 to 1 control (100 controls). This sample size was obtained using the StatCalc of the Epi-Info program version 7.2 for Windows to calculate the sample size in unpaired cases and controls, using the following criteria, based on the main factors associated with CKD described in studies such as that of (Poll et al., 2017) [1] and (Cajina & Gutiérrez, 2016) [5]: expected frequency of exposure in cases: 63.2%, expected frequency of exposure in controls: 30%, odds ratio to detect: 4, confidence level of 95%, statistical power of 80%, case/control ratio 1:2.

### Quantitative variables

Inferential statistics were used. Scaled results are expressed as the means and standard deviations. Categorical data such as sex are presented as proportions.



### Statistical analysis

A bivariate analysis compared the group of cases and controls with the chi-square test. The odds ratio was used to demonstrate the association of possible risk factors. The statistical package used was SPSS 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

## Results

### Participants

Fifty-one cases and 102 controls were included in the study.

### Baseline characteristics of the study population

The general characteristics of the population are presented in Table 1. A higher percentage was of cases in patients older than 60, and the male:female ratio was 1 to 1.19. Most of the patients came from rural areas, and most cases had primary education and obesity. According to the classification of CKD according to GFR in the population studied, it was found that in patients without CKD, stages G1 and G2 predominated with 14.7% and 85.3%, respectively. Patients with CKD presented stage G3 to G5, 27.5% G3a, 51% G3b, 5.9% G4, and 15.6% G5.

A total of 78% of patients with CKD are in stage G3, according to the KDIGO classification, corresponding to a moderate to severely decreased GFR. Likewise, a proportion of patients in stage G4 severely diminished and G5 had renal failure or ESRD.

### Risk factor analysis

#### Age and Sex

Of the total number of male patients with CKD, 32.5% were under 60 years of age, and 67.5% were greater than or equal to 60 years of age. In the controls, 53.5% were under 60 years of age, and 46.5% were greater than or equal to 60 years of age. Of the total number of women with CKD, 9.1% were under 60 years of age, and 90.9% were 60 years of age or older; 84.8% of the female controls were under 60 years of age, and 15.3% were 60 years of age or older. The prevalence of CKD is proportional to increasing age and is higher in those older than or equal to 60 years in both sexes ( $P < 0.001$ ). A statistically significant association with age was found [OR: 6.65 (3.14-14.09)  $P < 0.001$ ]. The prevalence of CKD was 78.4% in men, and an increased risk of CKD was demonstrated by almost five times with a significant association [OR 4.98 CI95% (2.30-10.82)  $P < 0.001$ ].

#### Origin and occupation

According to origin and occupation, of the total number of patients with CKD in rural areas, 71.1% were farmers, 2.6% were homemakers, 5.3% were merchants, and 21.3% were workers. While the controls, 6.3% are farmers, 55.6% are homemakers,

14.3% are merchants, 22.2% are workers, and 1.6% carry out professional activities. From the urban area, the cases correspond to 15.4% farmers, 7.7% homemakers, 23.1% merchants, and 53.8% workers. Among the controls, 41% are homemakers, 17.9% are merchants, 38.5% are workers, and 2.6% carry out professional activities.

CKD occurred in 74.5% of patients in rural areas. The occupation that predominated in the rural area was a farmer at 56.9%, followed by workers at 25.5%. Agricultural occupation showed an increased risk of suffering from CKD more than six times with a significant association [OR: 6.73 CI95% (2.67-16.95)  $P = 0.001$ ]. Origin was not significantly associated with CKD.

**Table 1.** Characteristic sociodemographic characteristics of the study group

	No. (n=153)	%
<b>Age (years)</b>		
< 60	87	56.9
≥ 60	66	43.1
<b>Sex</b>		
Men	83	54.3
Woman	70	45.8
<b>Origin</b>		
Rural	101	66
Urban	52	3.4
<b>Occupation</b>		
Farmer	33	21.6
loves of House	53	34.6
Businessman	21	13.7
Worker	44	28.8
Professional	two	1.3
<b>Scholarship</b>		
illiterate	14	9.2
Primary	90	58.8
Secondary	43	28.1
University	6	3.9
<b>body mass index</b>		
Weight normal	28	18.3
Overweight	56	36.6
Obesity	69	45.1

### Scholarship

Concerning schooling, in patients with CKD, it was found that 19.6% were illiterate, 68.6% had primary disease, and 11.8% had secondary disease. Among the controls, 3.9% had no education, 52.9% were primary, 37.3% were secondary, and 5.9% were university. It is evident in this study that most patients with CKD have primary schooling, which added to rurality, and the agricultural occupation demonstrates the social, cultural, and economic level of the population studied, associated with poorer health.



Illiterate schooling showed a more than 2-fold increase in the risk of CKD with a significant association [OR: 2.46, 95% CI (1.07-5.68)  $P = 0.003$ ].

### Nutritional condition

Regarding the nutritional status of patients with CKD, 35.3% had normal weight, 31.4% were overweight, and 33.3% were obese. Among the controls, 9.8% had normal weight, 39.2% were overweight, and 51% were obese. It is evident in this study that 6 out of 10 patients with CKD were overweight or obese. Obesity was shown to increase the risk of CKD by 2-fold with a significant association [OR: 2.08, 95% CI (1.03-4.18)  $P = 0.03$ ] (Figure 1).

### Family history

No association was found between a family history of kidney disease and the presence of CKD.

### Hypertension

Regarding hypertension associated with CKD, it was found that 51.6% of the study patients were hypertensive, 82.4% were cases, and 36.3% were controlled; 48.4% of the patients were not hypertensive; of these, 17.9% were cases and 63.7% were controls. This study showed that more than half of the patients presented arterial hypertension. Of the 51 patients diagnosed with CKD, 82.4% were hypertensive. Hypertensive patients were eight times more likely to suffer from CKD than patients who were not, with a significant association OR 8.19 (95% CI 3.59-19.71) ( $P = 0.001$ ). It is noteworthy that more than one-third of the controls (36.3%) were hypertensive.

### Mellitus diabetes

Concerning DM2 as a risk factor associated with CKD, it was found that 28.8% of patients had diabetes; of these, 51% were cases, and 17.6% were controlled; 71.2% of the patients did not have diabetes, of which 49% were cases and 82.4% were controls. Almost one-third of the patients had DM2, with a predominance of cases (51%). A statistically significant association was found; diabetic people had an almost five times greater chance of suffering from CKD than nondiabetic people, which was significantly associated with an OR of 4.85 (95% CI 2.29-10.26) ( $P = 0.001$ ).

### Dyslipidemia

Regarding dyslipidemia in the study population, it was found that 17.6% of the patients presented lipid alterations; of these, 15.7% of the cases and 18.6% of the controls. A total of 82.4% of patients did not have dyslipidemia. There was no association between dyslipidemia and chronic kidney disease (Figure 1).

### Heart disease

Regarding CVD, it was found that 17.6% of the patients studied had CVD; of these, 15.7% were cases, and 18.6% were controls; 82.4% of the patients did not have CVD; and 84.3% were cases and 81.4% were controls.

A total of 15.7% of patients with CKD had cardiovascular disease, and 84.3% did not. There was an association of risk factor type since patients with CVD had a four times greater chance of suffering from CKD than those who did not, which was significantly associated [OR: 4.40, 95% CI (1.05-18.38)  $P = 0.02$ ].

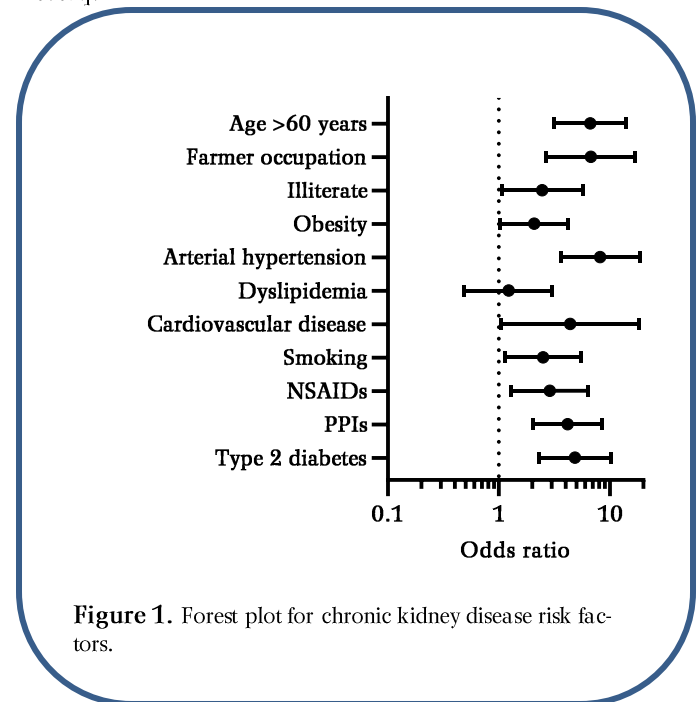


Figure 1. Forest plot for chronic kidney disease risk factors.

### Smoking

Regarding smoking, it was found that 22.2% of the studied population had a smoking habit, and 77.8% did not. In patients with CKD, 33.3% were smokers, and 66.7% were not smokers. In patients without CKD, 16.7% were smokers, and 83.3%. In this study, 33.3% of patients with CKD had a smoking habit, and 66.7% did not. A statistically significant difference was demonstrated ( $p=0.01$ ). There was an association between the type of risk factor; patients who smoked were almost 2.5 times more likely to suffer from CKD than those who did not have it (OR 2.5, 95% CI 1.14-5.45,  $P = 0.02$ ).

### NSAIDs

Regarding the use of NSAIDs, it was found that 66% of the population studied had consumed these drugs, and 34% had no history of consumption. In patients with CKD, 80.4% consumed NSAIDs. In patients without CKD, 58.8% were consumers of



NSAIDs, and 41.2% were not. In this study, 80.4% of patients with CKD consumed NSAIDs. Patients who consume NSAIDs are almost three times more likely to suffer from CKD than those who do not consume them, with a significant association [OR: 2.87, 95% CI (1.29-6.36),  $P=0.01$ ].

### Proton-pump inhibitor

Regarding the use of PPIs, it was found that 36.6% of the population studied had consumed these medications, and 63.4% had no history of consumption. In patients with CKD, 58.8% used PPIs. In patients without CKD, 25.5% were PPI consumers, and 74.5% were not. In this study, 58.8% of patients with CKD used PPIs. There was a significant association of risk factor type ( $P=0.01$ ); patients with PPI consumption had a four times greater chance of suffering from CKD than those who did not consume it, OR 4.17 (2.04-8.52)  $P=0.001$ .

## Discussion

This research demonstrates that the prevalence of CKD is proportional to increasing age and is higher in those over 60 years of age in both sexes ( $P=0.001$ ). These results agree with what was found by Cajina & Gutiérrez (2016) in Nicaragua [5], Robaina et al. (2013) in Argentina [6], and Francisco et al. (2007) in Spain [7], where he found 47.3% were men with a mean age of  $60.6 \pm 14.3$  years. Likewise, Sellarés (2017) mentions that in all the registries of kidney patients, the male sex represents approximately 60% of the patients in renal replacement therapy. In population studies, it is an independent prognostic factor for CKD.

This research shows the rural predominance of CKD in the municipality of Santa Teresa-Poblado Rural, which is related to the agricultural occupation that predominates in the population with CKD. Epidemiological studies clearly show that low social, cultural, and economic status is associated with poorer health, and CKD is not exempt from these circumstances. Likewise, Stanifer et al. (2016) [8] mention that rural agricultural communities in Central American countries face unique challenges related to CKD, where young male agricultural workers in these countries have very high rates of CKD of uncertain etiology. The results coincide with those of Díaz & Gallo (2007) [9], Nicaragua, at the Spain Hospital in Chinandega, and Cajina & Gutiérrez (2016) [5], Nicaragua, at a Tipitapa health post, demonstrating predisposing risk factors for IRC living in rural areas and being a farmer. These conditions of poverty are combined with illiteracy, a risk factor for chronic kidney disease in this study.

Epidemiological studies associate obesity with impaired kidney function and progression to ESRD (Kovesdy, Furth, Zoccali, & Committee, 2017) [10]; however, obesity and associated CKD are mainly preventable. Education and awareness

of the risks of obesity and adopting a healthy lifestyle can help prevent obesity and kidney damage.

The presence of arterial hypertension constitutes the most critical risk factor for CKD. These results agree with Guzmán-Guillén et al. (2014) [11], who found an association of CKD with HT PR: 2.21, and with de Francisco et al. (2007) [7], who found HT in 66.7% of patients with CKD. Poll et al. (2017) [1] mention that arterial hypertension has been documented as the leading risk factor for CKD, which is suffered by more than 75% of patients and is both a cause and a consequence of CKD.

Type 2 diabetes is a traditional factor for the development of CKD. These results agree with Robaina et al. (2013) [6], who found that 14.1% of CKD patients had DM. Likewise, Torres et al. (2017) [12] mention that DM is an important modifiable risk factor for the development of CKD since it is its main cause and constitutes frequent morbidity in nondiabetic nephropathy. It is estimated that one-third of patients with diabetes will develop kidney disease within 5 to 10 years after the diagnosis of DM. (BMJ, 2020) [13]. It is demonstrated in this study that CKD and DM are frequent chronic diseases and that they represent an important public health problem since they generate a large consumption of resources and require adequate coordination of the various professionals involved in their care to be addressed.

Regarding cardiovascular disease, Vallianou et al. (2019) [14] described that patients with advanced kidney disease, stage 4 or 5, are at high risk of CVD morbidity and mortality. For this reason, CKD has now been considered an independent risk factor for CVD and an equivalent coronary artery disease equivalent for all causes of mortality, as an association has been shown in the present study.

Smoking is an independent and transparent risk factor for CKD. It should be considered one of the most important modifiable risk factors, which is why tobacco abstinence is a priority recommendation for CKD (Achiardi et al., 2011) [15]. The same is true of the use of NSAIDs and the chronic intake of PPIs, factors that must be considered in the daily consultation of geriatric patients at risk. Future studies should explore the additive effect of risk factors and their relationship with the presence of chronic kidney disease.

## Conclusions

The factors that associate poverty with chronic kidney disease are illiteracy, obesity, residence in rural areas, and the farming profession. Traditional risk factors, such as hypertension, cardiovascular disease, and diabetes, were verified in this study. The use of PPIs has a higher risk of CKD than the use of NSAIDs.

### Abbreviations

NSAIDs: Nonsteroidal anti-inflammatory drugs.  
CVD: cerebral vascular event.



CKD: chronic kidney disease.  
AHT: Arterial hypertension  
PPIs: Proton Pump Inhibitors

## Supplementary information

Supplementary materials have not been declared.

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Does not apply.

## Author contributions

José Ángel Rivera Medina: Conceptualization, Data curation, Formal analysis, Funding, Research, Methodology, Project management, Resources, Software, Writing – original draft.

Kevin Duvan Quezada Jiménez: Conceptualization, supervision, validation, visualization, and writing: review and editing.

Javier José Somarriba Munguía: conceptualization, supervision, validation, visualization, and writing: review and editing.

Maritza Lissett Narváez Flores: Methodology, validation, supervision, writing: Review and editing.

All authors read and approved the final version of the manuscript.

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The authors provided research expenses.

## Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available from the corresponding author upon reasonable academic request.

## Statements

### Ethics committee approval and consent to participate

The HERSJ teaching committee approved this study of Carazo.

### Consent to publication

It does not apply when images or photographs of the physical examination or X-rays/tomographies/MRIs of patients are not published.

### Conflicts of interest

The authors report having no conflicts of interest.

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