



# Etiology of stage 5 chronic kidney disease: A multicenter observational study.

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# **Abstract**

**Introduction:** Chronic kidney disease (CKD) is a catastrophic condition and a public health problem in Ecuador. The present study aims to determine the prevalence of etiologies of stage 5 chronic kidney disease among patients in the public dialysis network in the city of Cuenca in March 2018.

**Materials and methods: A cross-sectional,** multicenter study was conducted. Data were collected from 458 patients using a questionnaire. Tabulation and statistical analysis were performed in Microsoft Office Excel 2016. The results were presented in simple distribution tables.

**Results:** The distribution by sex was 50.44% men and 49.46% women. The mean age was  $58.47 \pm 13.59$  years. The etiologies were: Diabetes Mellitus (41.92%), Arterial Hypertension (34.06%), Unknown Etiology (11.57%), Unrelated Glomerulopathies (3.06%), Obstructive Uropathy (2.4%), and the remaining pathologies (6.99%).

**Conclusions**: The main etiologies of stage 5 CKD were Diabetes Mellitus and Arterial Hypertension.

# **Keywords:**

Chronic Kidney Disease, final stage, etiologies.

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According to the "Global Burden of Disease A study published in 2013), from 1990--2010, global mortality from chronic kidney disease (CKD) ranked second in growth rate after HIV/AIDS. Thus, in 1990, it was the twenty-seventh leading cause of death, and by 2010, it had risen to eighteenth. The incidence of CKD has increased from the thirteenth leading cause in 1990 to the second leading cause in 2019 [1, 2].

Epidemiological data reflect this reality: in our region, the 2013 Latin American Registry of Dialysis and Kidney Transplantation (RLDTR) reported that "the prevalence of end-stage renal disease on renal replacement therapy (RRT) increased from 119 patients per million inhabitants (pmp) in 1991 to 669 pmp in 2013" [3]. Ecuador presented a prevalence of 529.8 pmp and an incidence of 177.6 pmp for the use of dialysis as RRT in the same year [3]. By 2022, with 19,327 patients in hemodialysis programs, the incidence rate was 206 patients per million inhabitants, and the prevalence was 1,074 patients per million inhabitants [4].

Furthermore, chronic kidney disease (CKD) is considered a catastrophic illness, making it a public health problem both in Ecuador and worldwide. It is estimated that CKD accounts for up to 3% of the annual healthcare budget in most countries. In Ecuador, a patient undergoing hemodialysis (HD) requires an annual expenditure of \$17,472.00 for the State and \$15,600.00 for peritoneal dialysis (PD), according to the "Ecuador National Renal Health Program 2015" [4, 5].

The Kidney Disease Improving Global Outcomes (KDIGO), in its latest Clinical Practice Guideline, published in 2012, defines chronic kidney disease as "Abnormalities of kidney structure and function, present for more than 3 months, with implications for health" [6].

In the 2002 KDIGO guidelines, the disease stages were defined solely on the basis of the glomerular filtration rate (GFR); however, the latest update has deemed it appropriate to integrate the etiology of CKD and albuminuria as indicators of severity. CKD consists of 5 stages; from the third stage onward, there is a significant decline in kidney function with a GFR less than 60 ml/min/1.73 m<sup>2</sup>, culminating in renal failure with a GFR less than 15 ml/min/1.73 m<sup>2</sup>, at which point renal replacement therapy (RRT) is necessary [6].

The importance of investigating the cause of CKD lies in targeted treatment and the obligation to inform patients about their prognosis. Diabetes mellitus (DM) and hypertension (HTN) are the main etiologies of CKD in all developed countries and in many developing countries. The Latin American Society of Nephrology and Hypertension (SLANH) states that DM is the leading cause of endstage CKD; its incidence is "correlated with the incidence and incidence rates of renal replacement therapy (RRT) (r=0.65; P < 0.05, and r=0.61; P < 0.05, respectively)" [3]. The Clinical Practice Guideline of the Ministry of Public Health (MSP) of Ecuador on "Prevention, diagnosis and treatment of chronic kidney disease", published in 2018, states that chronic kidney disease is associated with highly

prevalent chronic diseases, such as diabetes mellitus (30%), hypertension (25%), and glomerulopathies (20%) [ $\underline{\mathsf{Z}}$ ].

Additionally, infectious etiologies remain prevalent in low-income countries because of poor sanitation, inadequate access to safe drinking water, and high concentrations of disease vectors. Furthermore, environmental pollution, pesticides, analgesic overuse, herbal medicines, and the use of unregulated food additives contribute to the burden of CKD in developing countries [1].

In Ecuador, the Ministry of Public Health (MSP) lacks clear and concise information on the epidemiology of chronic kidney disease (CKD). All available data come from the Latin American Society of Nephrology and Hemotherapy (SLANH), which, through the Latin American Registry of Dialysis and Renal Transplantation (RLDTR), presents a synthesis of national registries of stage 5 CKD provided by the Nephrology Societies of 20 countries in the region affiliated with this institution. Therefore, this study aims to establish the prevalence of stage 5 chronic kidney disease etiologies in patients belonging to the public dialysis network in the city of Cuenca in March 2018, in addition to identifying the characteristics of the etiologies and determining their duration prior to the diagnosis of end-stage renal disease, to gain an overview of the local reality of this pathology.

# Materials and methods

### Studio design

This was an observational, cross-sectional study. The source is retrospective.

### Scenery

This study was conducted in three hemodialysis units in Azuay, Baxter, Unireas, and Dialilife, which are located in the city of Cuenca, Ecuador. The study period was from March 1, 2018, to March 31, 2018.

### **Participants**

Records of adult patients over 18 years of age with stage 5-D chronic kidney disease who were undergoing hemodialysis or peritoneal dialysis programs were included. Records of patients who did not report the etiology (including unidentified etiology) were excluded.

### **Variables**

The sociodemographic variables included age, sex, ethnicity, location of housing, body mass index, treatment modality, and etiology of kidney disease.

### Data sources/measurements

The source was indirect; institutional records from participating centers were used for data collection.

#### Biases

The surveys were administered in a standardized manner by the principal investigator via a preestablished guide approved in the research protocol. The information was independently reviewed by two researchers and recorded in duplicate. Only records with complete agreement were included.

#### Study size

The sample was probabilistic, with a prevalence of CKD of 1074 cases per million inhabitants in Ecuador. For the population of Azuay, with 801,609 inhabitants, this would mean 860 cases. With a 99% confidence level, an expected frequency of 50%, and a 5% confidence limit, the sample size was 375 cases.

#### Quantitative variables

The results for ordinal variables are presented as frequencies and percentages. The results for the scale variables are presented as averages. Scale variables were not converted into quantitative variables.

### Statistical analysis

Inferential statistics were used. Percentages were compared via the chi-square test. The results of the association analysis are presented as odds ratios and 95% confidence intervals. Statistical analysis was performed via SPSS version 31.0 (IBM Corp., 2024/2025).

# Results

### **Participants**

**A total of** 458 cases were included in the study, accounting for 100% of the sample size.

### Characteristics of the study population

Table <u>1</u> shows that, out of a total of 458 patients, 50.44% (231) were male and 49.46% (227) were female. The mean age was  $58.47\pm13.59$  years. The 71–80 years age range was the most representative, with 28.82% (132), and the 21–30 years age range was the least represented, with 4.37% (20) of patients.

Compared with rural areas, urban areas had the greatest number of affected individuals, 57.42% (263). Among the 81.44% (373) of patients, 37.34% (171) had a normal BMI, 30.79% (141) were overweight, and 12.23% (56) were obese. The most frequently used renal replacement therapy (RRT) was hemodialysis, at 87.77% (402).

### **Etiology**

Table 2 presents the KDIGO classification of CKD etiologies. A total of 47.38% (217) of the records corresponded to glomerular diseases, 34.28% (157) to vascular diseases, 11.57% (53) to unknown etiologies, 4.15% (19) to tubulointerstitial diseases, 1.53% (7) to cystic and congenital diseases, and 1.09% (5) to other unclassified etiologies. When these groups were broken down, 18 causes were found, the most frequent being diabetes mellitus in 41.92% (192) of patients, arterial hypertension in 34.06% (156), unknown etiology in 11.57%

(53), unclassified glomerulopathy in 3.06% (14), obstructive uropathy in 2.4% (11) and other pathologies in 6.99% (32) of patients.

Among patients with diabetes mellitus (DM), 39.58% (76) were between 61 and 70 years old, and 50.52% (97) were female. Among patients with hypertension (HTN), the predominant age group was 71--80 years, accounting for 32.05% (50) of the patients, and 55.13% (86) were female. In contrast, patients with an unknown etiology were predominantly young, with 24.53% (13) between 31 and 40 years old, and were mostly male (58.49%; 31). Among the patients with obstructive nephropathy, 91% (10) were men due to prostate pathology, unlike the patients with systemic lupus erythematosus, who were all women.

Regarding the duration of the underlying disease prior to the diagnosis of stage 5 CKD, 69.4% (34) of 49 patients with diabetes mellitus (DM) had disease for more than 10 years; however, the duration was not specified for 18.4% (9). With respect to hypertension (HTN), 25.3% (19) of 75 patients had hypertension for more than 10 years, 18.7% (14) had hypertension for less than one year, and 17.3% (13) did not specify the duration (Figure 1). Finally, of the 24.45% (112) of patients, 44.64% (50) presented with multiple probable etiologies, with the combination of HTN and DM being the most common at 60% (30). No data were found on a history of smoking.

# Discussion

The results of this study provide epidemiological information on stage 5 chronic kidney disease (CKD) in the adult population belonging to the public dialysis network of the city of Cuenca. In this study, the distribution was similar between sexes, with 50.44% men and 49.46% women; regarding age, the mean was 58.47 ± 13.59 years, with the highest frequency between 71 and 80 years. A meta-analysis published in 2016, conducted worldwide, revealed that "the mean prevalence of CKD in men (95% CI) for studies using stages 3–5 was 8.1% (6.3–10.2), whereas the prevalence of CKD in women was 12.1% (10.6–13.8)"; this finding indicates a tendency for CKD to be more prevalent in women. Our study revealed similar frequencies in men and women. In the same study, the age range of 70 years or older was the most representative, which is consistent with our reality [8].

**Table 1.** General description of the sample.

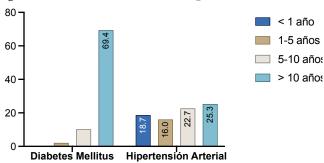
Variable	Frequency n=458 (%)
Male sex	231 (50.44%)
Age	
21-30 years old	20 (4.37%)
31-40 years	29 (6.33%)
41-50 years	55 (12.01%)
51-60 years	92 (20.09%)
61-70 years	130 (28.38%)
71-80 years	132 (28.82%)
Geographical location of the dwelling	
Rural	195 (42.58%)
Urban	263 (57.42%)
Body mass index	
Low weight	5 (42.58%)

Normal	171 (37.34%)	
Overweight	141 (30.79%)	
Obesity I	37 (8.08%)	
Obesity II	12 (2.62%)	
Obesity III	7 (1.53%)	
No data	85 (18.56%)	
Modality of Renal Replacement Therapy		
Hemodialysis	402 (87.77%)	
Peritoneal dialysis	56 (12.22%)	

Table 2. Etiology in the study group .

Glomerular Diseases	
Type 2 diabetes mellitus	41.92%
Undiagnosed glomerulopathy	3.06%
Diffuse membranous glomerulonephritis	0.87%
Systemic lupus erythematosus	0.87%
Focal segmental glomerulosclerosis	0.66%
Vascular diseases	
High blood pressure	34.06%
Wegener's granulomatosis	0.22%
Tubulointerstitial diseases	
Obstructive uropathy	2.4%
Toxic nephropathy	2.0%
Undiagnosed tubulointerstitial nephropathy	0.66%
Drop	0.66%
Cystic and congenital diseases	
Polycystic kidney disease	0.87%
Congenital malformation of the urinary tract	0.66%
Other causes	
Failure and rejection of the transplanted kidney	0.44%
Renal tuberculosis	0.44%
Renal failure following procedures	0.22%

Figure 1. Evolution time of the main ones etiologies .



At the Latin American level, a Chilean study conducted in urban primary care centers revealed that, among patients diagnosed with CKD, the disease was significantly more common in women than in men [9], considering that the methodology of both studies included patients in stages 3, 4, and 5, which differs from our findings.

At the local level, Guzmán K et al., in their study of patients with chronic kidney disease (CKD) treated at the Internal Medicine Clinic of the José Carrasco Arteaga Specialty Hospital (HEJCA) in the city of Cuenca, reported that 81.13% were from urban areas and 18.86% were from rural areas [10], which is a greater difference than that reported in our study (57.42% vs. 42.58%). This is because dialysis centers receive patients from various health institutions, including the Ministry of Public Health (Vicente Corral Moscoso Hospital - HVCM), which serves a high volume of patients from rural areas. This allows for a more balanced ratio between the rural and urban populations [11].

An epidemiological study conducted in Mexico in 2010, which compiled monthly reports from dialysis programs totaling 31,712 cases, identified diabetes mellitus (DM) as the primary etiology of stage 5 chronic kidney disease (CKD), at 48.5%, followed by hypertension (HTN) at 19%, chronic glomerulopathies at 12.7%, undetermined causes at 7.4%, and obstructive uropathy at 0.7%, which is consistent with our results [12]. Notably, in this study, nephropathy of unknown cause ranked third, with men aged 31--40 years being the most affected. This may be due to uninvestigated clinical pathologies or factors related to agricultural activities, exposure to heavy metals, heat stress, diet, or the consumption of herbal supplements, as mentioned in the systematic review by Lunyera J et al. (2016) [13]. It has been proposed that "diabetes mellitus overall is the most common cause of glomerulopathies, such as end-stage renal disease" [14]. It is also known that in Latin America, the "overall rate of incident diabetic patients requiring renal replacement therapy was 58 pmp, lower than that reported by the United States Renal Data System (158.4 pmp), but double that of the European ERA/EDTA Registry (24 pmp)" [3, 15]. This situation can be explained by the higher prevalence of diabetes mellitus than hypertension in the country. According to data from the Ministry of Public Health, in 2016, diabetes was the third leading cause of death, whereas hypertension was the eleventh leading cause, just below chronic kidney disease [1, 2].

With respect to BMI, overweight was observed in 30.79% of patients, similar to the 39.5% reported by Gorostidi M et al., followed by obesity in 22.6% of patients (15); this relationship was supported in an investigation by Torracchi A et al. (2007) carried out at the HVCM, which demonstrated a significant association between CKD and overweight, RP= 2.014 (95% CI 1.09-3.70, P=0.02) [15].

Martín N et al. (2014) reported that a longer duration of hypertension is associated with increased progression and complications in patients with chronic kidney disease (CKD), with six patients having a duration of hypertension of 0- 30 years compared with one patient with a duration of hypertension of 0- 15 years before CKD [16]. The data obtained showed that the majority (25.3%) had suffered from hypertension for more than 10 years before CKD diagnosis; however, a significant percentage (18.7%) developed hypertension in less than one year. This situation may be due to a late diagnosis of hypertension or the manifestation of hypertension secondary to kidney damage. Furthermore, 69.4% had been diagnosed with diabetes mellitus (DM) for more than 10 years, which is consistent with the natural history of the disease and with the findings of a study by Padilla R. et al. (2015), which revealed an average of 21.25 years (95% CI; 18.65–23.76) before stage 5 CKD.

Among the limitations of our study are insufficient data for variables such as BMI, family history of CKD, duration of illness before CKD, and smoking, which complement the primary purpose of the research, and the inherent bias of any retrospective study that uses records or medical histories, thus requiring greater emphasis on this approach. This situation aligns with the SLANH, which maintains that Ecuador, like Bolivia, Brazil, Panama, Paraguay, Peru, and Venezuela, contributes only partial data to the RLDTR [3]. Furthermore, the lack of knowledge regarding the diagnostic methods for determining and reporting the etiology of CKD (biopsy, laboratory tests, medical history, etc.) underscores the accuracy of these methods.

This research encompasses the entire population of patients undergoing chronic dialysis in Cuenca, allowing the results to be extrapolated to the city's context. Furthermore, understanding the underlying causes of these conditions enables timely detection and treatment to prevent progression to end-stage renal disease (ESRD), which significantly affects the quality of life of patients, their families, and society. Future studies should monitor glycated hemoglobin and cardiovascular risk, and the presence of neuropathy, using prospective designs to assess mortality in these patients [17-19].

# Conclusion

The results of this study revealed that in stage 5 CKD patients, the mean age was  $58.47 \pm 13.59$  years, with the highest frequency between 71 and 80 years, and a slight predominance in males residing in urban areas. The primary etiology was diabetes mellitus (41.92%), followed by hypertension (34.06%), unknown etiology (11.57%),

unclassified glomerulopathies (3.06%), obstructive uropathies (2.4%), and other pathologies (6.99%). In patients with diabetes mellitus and hypertension, a disease duration of more than 10 years before the diagnosis of stage 5 CKD was prevalent. Among the 24.45% of patients, 44.64% presented with multiple probable etiologies, with the combination of hypertension and diabetes mellitus being the most common (60%).

#### **Abbreviations**

DM: diabetes mellitus. CKD: chronic kidney disease. BMI: Body mass index.

### **Supplementary information**

The supplementary materials have not been included.

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### **Authors' contributions**

Gabriel Alejandro Cepeda Flores: Conceptualization, data curation, research, visualization, original draft writing.

**Dana Isabel Reyes Encalada:** Conceptualization, data curation, research, visualization, original draft writing.

**César Toral Chacón**: Conceptualization, data curation, formal analysis, project management, software, validation, visualization, writing—review and editing. **Carla Salgado**: Conceptualization, formal analysis, methodology, project management, resources, software, supervision, validation, writing—review and editing.

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

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#### Availability of data or materials

Not applicable.

### Statements

### Ethics committee approval and consent to participate

The study was approved by the Bioethics Committee of the Faculty of Medical Sciences of the University of Azuay.

### **Consent for publication**

This does not apply when specific patient images, radiographs, or photographs are not published.

### **Conflicts of interest**

The authors declare that they have no conflicts of interest.

### Use of generative Al

The authors declare that they used generative AI responsibly, without replacing their critical thinking, experience, and judgment. The AI was used under supervision and control to develop the discussion section. The use of the AI tool maintains the privacy and confidentiality of data and contributions, including published and unpublished manuscripts, as well as any personally identifiable information. The journal's policies, which permit the use of generative AI only in the introduction and discussion sections, have been followed.

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The accuracy, integrity, and impartiality of all Al-generated results were carefully reviewed and verified to ensure that the manuscript reflects an authentic and original contribution.

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