Burden of Chronic Kidney Disease in Peru: A Population-based Study

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& the CRONICAS Cohort Study Group

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I. Overview

• CKD’s silent progression, association with multiple chronic diseases, and high treatment costs make CKD a public health concern
  – WHO dialysis cost-effectiveness estimate: $108,600 USD per DAILY \(^1,2\)

• Peru was selected due to a unique confluence of scenarios
  – Diverse socioeconomically, climactically and geographically
  – Rapid population growth
  – Rising prevalence of CVD risk factors
  – ~42% of Peruvians are insured. 30% have insurance access to RRT \(^3,4\)

• Limited information on CKD burden in Peru
  – 1990: CKD in Lima was ~12.2 / 100,000 \(^5\)

• Our Study: Examined the prevalence of CKD and associated risk factors in two Peruvian cities
II. Methods

• **Design**: Cross-sectional study nested within ongoing CRONICAS cohort study (n=3,000)

• **Participants**: Random selection using census data. Recruitment into site, gender, age group strata.

• **Inclusion**: Full-time residence in the area, ability to understand study procedures, informed consent

• **Data Collection**: Completed by trained fieldworkers. Door-to-door. Samples processed by MetLab in Lima

• **Analysis**: Multivariate Poisson regression used to determine prevalence ratios and assess relationship between CKD and hypothesized risk factors

  – CKD = estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m$^2$ or proteinuria (protein/creatinine ratio) ≥150 mg/g creatinine, or both
### III. Results

- 404 participants
- Median age 54.8 yrs (IQR 44.9-64.8)

#### Prevalence

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent (%)</th>
<th>Count</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD *</td>
<td>16.8</td>
<td>68</td>
<td>13.5 – 20.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9.9</td>
<td>40</td>
<td>7.4 – 13.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29.2</td>
<td>118</td>
<td>25.1 – 34.0</td>
</tr>
</tbody>
</table>

#### * CKD (N = 68) Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Mean</th>
<th>Count</th>
<th>Range</th>
<th>Cut point</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR</td>
<td>40.1 mL/min/1.73 m²</td>
<td>8</td>
<td>15.0 – 57.7 mL/min</td>
<td>&lt;60 ml/min/1.73 m²</td>
</tr>
<tr>
<td>Protein/Creatinine</td>
<td>345.71</td>
<td>64</td>
<td>151.5 – 1,840.9</td>
<td>≥150 mg/g creatinine</td>
</tr>
</tbody>
</table>

- 50.2% male; 49.8% female
- 203 Lima; 201 Tumbes
Poisson Analysis

• **Multivariate Poisson** (independently associated with CKD)
  – Older age
  – Female gender
  – Living in Lima
  – Diabetes
  – Wealth below Peruvian poverty level

• Additional variables significant only in unadjusted Poisson
  – Hypertension
  – Lower education level
  – Greater levels of insulin resistance (HOMA-IR)
    • A measure of pancreatic islet cell function
## Participants with and without CKD

<table>
<thead>
<tr>
<th></th>
<th>No CKD N = 336, 83.2%</th>
<th>CKD N= 68, 16.8%</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year, median (IQR)</td>
<td>53.5 (43.6 – 63.2)</td>
<td>59.6 (50.5 – 69.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>182 (54.2)</td>
<td>21 (30.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Location, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lima</td>
<td>161 (47.9)</td>
<td>42 (61.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Tumbes</td>
<td>175 (52.1)</td>
<td>26 (38.2)</td>
<td></td>
</tr>
<tr>
<td>Education (yrs), n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary or less</td>
<td>138 (41.1)</td>
<td>41 (60.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Secondary</td>
<td>139 (41.4)</td>
<td>14 (20.6)</td>
<td></td>
</tr>
<tr>
<td>&gt; Secondary</td>
<td>59 (17.6)</td>
<td>13 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Wealth Index, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>67 (19.9)</td>
<td>7 (10.3)</td>
<td>0.17</td>
</tr>
<tr>
<td>Medium</td>
<td>134 (39.9)</td>
<td>30 (44.1)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>135 (40.2)</td>
<td>31 (45.6)</td>
<td></td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>27 (8.0)</td>
<td>13 (19.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension, median (IQR)</td>
<td>89 (26.5)</td>
<td>29 (42.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HOMA-IR, median (IQR)</td>
<td>1.96 (1.15 – 3.35)</td>
<td>2.18 (1.12- 3.67)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
CKD prevalence stratified by sex & age

Estimated prevalence of CKD

- CKD in Females
  - Age 35-44
  - Age 45-54
  - Age 55-64
  - Age >=65

- CKD in Males
  - Age 35-44
  - Age 45-54
  - Age 55-64
  - Age >=65
Stratification by gender

**CKD in Males**

- **Study sites**
  - Lima: 103, 13.6 (08.3, 22.2)
  - Tumbes: 100, 07.0 (03.4, 14.4)

- **Diabetes**
  - No: 185, 10.3 (06.7, 15.7)
  - Yes: 18, 11.1 (02.9, 42.6)

- **Hypertension**
  - No: 152, 09.9 (06.1, 16.0)
  - Yes: 51, 11.8 (05.5, 25.1)

- **Dyslipidemia**
  - No: 54, 09.3 (04.0, 21.5)
  - Yes: 149, 10.7 (06.7, 17.1)

- **Inflammation**
  - No: 60, 08.3 (03.6, 19.4)
  - Yes: 143, 11.2 (07.0, 17.8)

- **FRS classification**
  - Low: 67, 04.5 (01.5, 13.6)
  - Intermediate: 67, 07.5 (03.2, 17.5)
  - High: 69, 18.8 (11.5, 30.9)

- **Overall**: 203, 10.3 (06.9, 15.5)

**CKD in Females**

- **Study sites**
  - Lima: 100, 28.0 (20.4, 38.4)
  - Tumbes: 101, 18.8 (12.5, 28.3)

- **Diabetes**
  - No: 179, 20.1 (15.0, 27.0)
  - Yes: 22, 50.0 (32.6, 76.7)

- **Hypertension**
  - No: 134, 17.9 (12.4, 25.8)
  - Yes: 67, 34.3 (24.6, 47.9)

- **Dyslipidemia**
  - No: 21, 28.6 (14.3, 57.1)
  - Yes: 180, 22.8 (17.4, 29.8)

- **Inflammation**
  - No: 40, 17.5 (08.9, 34.6)
  - Yes: 161, 24.8 (19.0, 32.5)

- **FRS classification**
  - Low: 124, 17.7 (12.1, 26.0)
  - Intermediate: 57, 33.3 (23.0, 48.3)
  - High: 20, 30.0 (15.1, 59.6)

- **Overall**: 201, 23.4 (18.2, 30.1)
Stratification by location

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>CKD in Lima</th>
<th>Estimated Prevalence (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>100</td>
<td>28.0 (20.4, 38.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Male</td>
<td>103</td>
<td>13.6 (08.3, 22.2)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>186</td>
<td>18.8 (13.9, 25.4)</td>
<td>0.02</td>
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<tr>
<td>Yes</td>
<td>17</td>
<td>41.2 (22.9, 74.0)</td>
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</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>145</td>
<td>17.2 (12.1, 24.7)</td>
<td>0.05</td>
</tr>
<tr>
<td>Yes</td>
<td>58</td>
<td>29.3 (19.6, 43.9)</td>
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</tr>
<tr>
<td>Dyslipidemia</td>
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<td></td>
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<tr>
<td>No</td>
<td>35</td>
<td>17.1 (08.2, 35.9)</td>
<td>0.58</td>
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<tr>
<td>Yes</td>
<td>168</td>
<td>21.4 (16.0, 28.6)</td>
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<tr>
<td>Inflammation</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>46</td>
<td>10.9 (04.7, 25.1)</td>
<td>0.08</td>
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<tr>
<td>Yes</td>
<td>157</td>
<td>23.6 (17.8, 31.3)</td>
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</tr>
<tr>
<td>FRS classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>96</td>
<td>17.7 (11.5, 27.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>Intermediate</td>
<td>63</td>
<td>23.8 (15.3, 37.2)</td>
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<tr>
<td>High</td>
<td>44</td>
<td>22.7 (13.1, 39.4)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>203</td>
<td>20.7 (15.8, 27.1)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>CKD in Tumbes</th>
<th>Estimated Prevalence (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>101</td>
<td>18.8 (12.5, 28.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Male</td>
<td>100</td>
<td>07.0 (03.4, 14.4)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>178</td>
<td>11.2 (07.4, 17.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
<td>26.1 (12.9, 52.7)</td>
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<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>141</td>
<td>09.9 (06.0, 16.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Yes</td>
<td>60</td>
<td>20.0 (12.0, 33.3)</td>
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</tr>
<tr>
<td>Dyslipidemia</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40</td>
<td>12.5 (05.4, 28.7)</td>
<td>0.93</td>
</tr>
<tr>
<td>Yes</td>
<td>161</td>
<td>13.0 (08.7, 19.5)</td>
<td></td>
</tr>
<tr>
<td>Inflammation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>54</td>
<td>13.0 (06.5, 26.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Yes</td>
<td>147</td>
<td>12.9 (08.5, 19.7)</td>
<td></td>
</tr>
<tr>
<td>FRS classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>95</td>
<td>08.4 (04.3, 16.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Intermediate</td>
<td>61</td>
<td>14.8 (08.0, 27.1)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>45</td>
<td>20.0 (11.1, 36.1)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>201</td>
<td>12.9 (09.0, 18.5)</td>
<td></td>
</tr>
</tbody>
</table>
IV. Take Home Points

1. Observed burden of CKD supports that chronic disease is also a problem in LMIC

2. Risk factors for CKD seen in USA were also associated with CKD in our sample population

3. Geographical location and environmental factors may influence CKD prevalence

4. Poverty and social deprivation are associated with CKD
Our observed CKD burden supports that chronic disease is also a problem in LMIC

- Our CKD estimate (16.8%) is similar to that observed in other non-Hispanic countries:
  - USA and Iran: 13-18% \(^6,7\)
  - China, Japan, Korea: 14-22% \(^8-10\)

- Other Latin American countries: \(^11-13\)
  - El Salvador and Nicaragua: 12.7%
  - Mexico: 9.2%
  - Chile: 14.2%
(2) Risk factors for CKD seen in developed countries were similar in our population

- Females and older age were both independently associated with CKD
  - Consistent with USA and Iran \(^6,7\)
  - Inconsistent with Nicaragua & Sri Lanka (M > F)

- Significant independent association with vascular disease risk factors (e.g., HTN and DM) was noted among females and older patients

Note: Mechanisms underlying sex difference in CKD epidemiology and CKD progression remain unclear and may involve a differential impact of traditional risk factors and environmental influences \(^{14}\)
(3) Geographical location and environmental factors may influence CKD prevalence

- Pesticides - Enhance progression to CKD \textsuperscript{11, 15, 16}

- High altitude - “Protective” against CKD progression
  - High altitude is associated with higher levels of eGFR \textsuperscript{17}
  - Lima and Tumbes are approximately at sea level; however, Lima site has 50% within-country migrant population from high altitude Andean region
  - Lima:
    - Average eGFR was higher compared to Tumbes
    - Smaller number of eGFR <60 ml/min/1.73 m\textsuperscript{2}
(4) Poverty & social deprivation are associated with CKD

- All sites fall below the average socioeconomic indicators for Peru and Lima
  - Access to healthcare in Lima 37% & Tumbes 50%

- Insurance reported is likely government subsidized insurance schemes which cover basic services such as immunizations, maternal health, and large ID programs (e.g., TB & HIV).
  - Thus, access to general medical care where CKD can be detected and managed is expected to be even lower
V. Call to Action

- High CKD prevalence (likely undiagnosed) identified

- CKD’s silent progression, association with multiple chronic disease diseases, and high treatment costs, make CKD a public health concern

- This study makes a call to:
  - Increase national surveillance that will influence policies aimed at
    - preventing CKD from escalating in Peru
      Insurance and dialysis is out of reach for most
  - Develop interventions aimed at
    - reducing CKD prevalence
    - managing existing cases of disease
VI. Funding & Thanks

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- The CRONICAS-UPCH & PRISMA teams for participant care
- Faculty of Weill Cornell Medical College, Drs. Oliver Fein and Madelon Finkel, for encouraging and supporting my research pursuits
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- Drs. Miranda and Feldman, the co-senior authors, who guided this project and senior student mentor Dr. Joseph Kuo, for his incite on data analysis

FINANCIAL DISCLOSURE

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References


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Study Variables

- **CKD**: glomerular filtration rate (eGFR) <60 ml/min/1.73 m$^2$ or proteinuria (protein-creatinine ratio) ≥150 mg/g creatinine, or both
- **Diabetes mellitus**: fasting plasma glucose ≥126 mg/dL or self-reported physician diagnosis or use of anti-diabetic medications
- **Hypertension**: systolic blood pressure (SBP) of ≥140 mmHg, a diastolic blood pressure (DBP) of ≥90 mmHg, receipt of anti-hypertensive therapy at the time of enrollment, or self-report of a diagnosis by a physician
- **Insulin resistance**: assessed using the homeostasis model assessment (HOMA-IR)
- **Framingham risk score**: calculated from National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III algorithm and based on six cardiovascular risk factors: age, gender, total cholesterol, HDL-cholesterol, systolic BP and smoking status. 10-year risk of coronary events was divided into three levels of risk: low (<10%), intermediate (10-20%), and high (>20%)
- **Socioeconomic status**: assessed using a wealth index based upon current occupation, household income, assets and household facilities
- **Smoking**: categorized as current, former, or never
- **Alcohol consumption**: categorized into non-current and current drinkers
- **Body mass index (BMI)**: calculated as weight in kilograms divided by height in meters squared
Strengths and Limitations

• **Strengths:**
  – High quality data collection and disease outcome surveillance
  – High response rate within ancillary CKD component
  – Standard lab methods used

• **Limitations:**
  – Cross sectional design
  – Additional RF could have been examined; e.g., environmental
  – Small sample size, limiting detection of smaller RF’s
  – Lead-time bias
Addressing the CKD Problem in Peru

• Define the problem and the players
  – Stakeholder analysis
  – Thorough examination of the prevalence

• Prevention
  – Primary: Behavior Modification
  – Secondary: Surveillance and Screening
  – Secondary/ Tertiary: CKD Treatment & Management
Local Peruvian Infrastructure

- La Universidad Peruana Cayetano Heredia
- San Marcos
- CRONICAS, Centro de Excelencia
- PRISMA

Peruvian National and Latin America Focused Organizations

- The Peruvian Ministry of Health (MOH)
- Peruvian Society of Nephrology (PSN)
- Pan American Health Organization (PAHO)
- Latin American Society of Nephrology
- Latin American Dialysis and Kidney Transplant Registry (SLAHN)
- Spanish Society of Nephrology

International Organizations

- National Kidney Foundation
- Kidney Disease: Improving Global Outcomes (KIDIGO)
- International Society of Nephrology (ISN)