# Urbanization and kidney dysfunction in Brazilian indigenous people: a burden for the youth

Orlando Vieira Gomes<sup>1,2\*</sup>, Manoel Pereira Guimarães<sup>2</sup>, Jandir Mendonça Nicacio<sup>1,2</sup>, Leela Morena<sup>2</sup>, Antônio Marconi Leandro da Silva<sup>2</sup>, Jeová Cordeiro de Morais Junior<sup>2</sup>, Carlos Dornels Freire de Souza<sup>2</sup>, Manoel Barral-Netto<sup>3</sup>, João Augusto Costa Lima<sup>4</sup>, Anderson da Costa Armstrong<sup>1,2</sup>

# **SUMMARY**

**OBJECTIVE:** The aim of this study was to investigate whether the degree of urbanization influences the prevalence of chronic kidney disease in Brazilian indigenous people.

**METHODS:** This is a cross-sectional study conducted between 2016 and 2017 in northeastern Brazil and includes individuals aged between 30 and 70 years from two specific indigenous groups who volunteered to participate in the study: the Fulni-ô people (lowest degree of urbanization) and the Truká group (greater degree of urbanization). Cultural and geographical parameters were used to characterize and measure the magnitude of urbanization. We excluded individuals with known cardiovascular disease or renal failure who required hemodialysis. Chronic kidney disease was defined as a single measurement of an estimated glomerular filtration rate <60 mL/min/1.73 m<sup>2</sup> using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.

**RESULTS:** A total of 184 indigenous people from the Fulni-ô group and 96 from the Truká group with a median age of 46 years (interquartile range: 15.2) were included. We found a chronic kidney disease rate of 4.3% in the total indigenous population, generally affecting an older population: 41.7% over 60 years old (p<0.001). The Truká people had a chronic kidney disease prevalence of 6.2%, with no differences in kidney dysfunction across age groups. The Fulni-ô participants had a chronic kidney disease prevalence of 3.3%, with a higher proportion of kidney dysfunction in older participants (of the six Fulni-ô indigenous people with chronic kidney disease, five were older).

**CONCLUSION:** Our results suggest that a higher degree of urbanization seems to negatively influence the prevalence of chronic kidney disease in Brazilian indigenous people.

KEYWORDS: Chronic kidney disease. Urbanization. Indigenous peoples.

## INTRODUCTION

Chronic kidney disease (CKD) is one of the most important public health concerns of the century, and it is known to be associated with high rates of mortality and social costs<sup>1</sup>. It is characterized by severe, irreversible kidney damage with a reduction in glomerular filtration rate of <60 mL/min/1.73 m<sup>2</sup> or a urinary albumin-to-creatinine ratio of <sup>3</sup>30 mg/g<sup>2</sup>. Previous studies have shown an increasing prevalence of CKD among indigenous people. When comparing outcomes with the general population, indigenous communities present higher mortality rates<sup>3</sup>.

Similar to other colonized indigenous population<sup>3</sup>, Brazilian indigenous people have undergone an accelerated process of

nutritional and epidemiological transition characterized by reduced physical activity and incorporation of new cultural habits. These factors have promoted the emergence of chronic diseases, such as CKD, and risk factors, such as obesity, hypertension, hyperglycemia, dyslipidemia, and diabetes, among indigenous people<sup>4-6</sup>. However, the literature describing the prevalence and determinants of CKD in Brazilian indigenous people is still scarce.

The Project of Atherosclerosis among Indigenous Populations (PAI) is a population-based study conducted in the Northeast Region of Brazil. The aim of this project was to assess cardiovascular health in indigenous groups with different degrees

<sup>4</sup>John Hopkins University – Baltimore (MD), USA.

\*Corresponding author: orlandopetro@msn.com

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<sup>&</sup>lt;sup>1</sup>Universidade do Estado da Bahia, Postgraduation Program in Human Ecology and Socio-Environmental Management – Juazeiro (BA), Brazil.

<sup>&</sup>lt;sup>2</sup>Universidade Federal do Vale do São Francisco, School of Medicine - Petrolina (PE), Brazil.

<sup>&</sup>lt;sup>3</sup>Oswaldo Cruz Foundation, Instituto Gonçalo Muniz – Salvador (BA), Brazil.

of urbanization. Between 2016 and 2017, the PAI study recruited 999 individuals, with no known previous cardiovascular event, who were inhabitants of the following three communities in the São Francisco River basin: two indigenous tribes (the less urbanized Fulni-ô and the more urbanized Truká people) and an urbanized non-indigenous control group from the same area<sup>4</sup>.

For this report, we exclusively assessed indigenous participants in the PAI study with available estimated glomerular filtration rate (eGFR) and clinical data to describe the prevalence of CKD and associated risk factors in both Brazilian indigenous communities living in different degrees of urbanization. Our hypothesis was that the group with a high degree of urbanization would have the highest prevalence of CKD.

# **METHODS**

The PAI study was approved by the National Research Ethics Council (CONEP number 1.488.268), the National Indigenous Foundation (Fundação Nacional do Índio [FUNAI]; process number 08620.028965/2015-66), and the indigenous leaders of both participating groups. All participants provided written informed consent before enrollment in the study.

#### Study design and recruiting

The PAI study has been described previously<sup>4</sup>. Briefly, it is a descriptive, cross-sectional study composed of two specific indigenous groups from the Sao Francisco Valley in the northeast of Brazil (Figure 1). These groups were assessed between 2016 and 2017, and then stratified by degree of urbanization: the Fulni-ô people with a low level of urbanization and the Truká group with a high level of urbanization. The classification of the degree of urbanization was



Figure 1. Geographical locations of the Truká and Fulni-ô groups.

based on the following group characteristics: geographical location, maintenance of traditional culture, proximity to and contact with cities, and influence of the city on the group's dynamics<sup>7,8</sup>.

The PAI study included individuals aged between 30 and 70 years who voluntarily agreed to participate in the study. Those with clinically manifested heart failure, history of coronary or cerebrovascular vascular diseases requiring hospitalization, renal failure on dialysis, or a history of surgery for peripheral arterial disease or heart disease were excluded.

The current analysis was carried out as an ancillary study of the PAI study, assessing participants with complete data on kidney function. In total, we analyzed 280 individuals: 184 (65.7%) from the Fulni-ô group and 96 (34.3%) from the Truká group.

# Sociodemographic and anthropometric parameters

We registered sex as a binary variable (male/female). Age was computed as a continuous variable in years, as well as categorized within four proportional groups (30–39, 40–49, 50–59, and 60–70 years). Individuals were classified according to body mass index as underweight (<18.5), normal ( $\geq$ 18.5 and <25), overweight ( $\geq$ 25 and <30), and obese ( $\geq$ 30). Obesity was subdivided into categories: class 1 (30 to < 35), class 2 (35 to <40), and class 3 "severe" obesity (>40)<sup>9</sup>.

#### **Clinical parameters and laboratory testing**

Hypertension was defined as systolic blood pressure  $\geq$ 140 mmHg, diastolic blood pressure  $\geq$ 90 mmHg, or taking hypertension medications<sup>10</sup>. Diabetes was diagnosed when HbA1c was <sup>3</sup>6.5% or using diabetes medications<sup>11</sup>. Dyslipidemia was established if the participant was using hypolipidemic medication or if at least one of the following criteria was met: reduced high-density lipoprotein cholesterol, a level <40 mg/dL in men or 50 mg/dL in women; hypertriglyceridemia, a triglyceride level >150 mg/dL; and hypercholesterolemia, an low-density lipoprotein cholesterol >160 mg/dL<sup>12</sup>.

Estimated glomerular filtration rate was calculated using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation without correction for race. According to the 2012 KDIGO criteria<sup>2</sup>, we classified the participants into three categories: normal/high (G1) (eGFR: ≥90 mL/min/1.73 m<sup>2</sup>), mildly decreased excretory renal function (G2) (eGFR: 60–89 mL/min/1.73 m<sup>2</sup>), and substantially reduced (G3) (eGFR: <60 mL/min/1.73 m<sup>2</sup>). We defined CKD as a single measurement of eGFR <60 mL/min/1.73 m<sup>2</sup>.

#### **Statistical analysis**

The following statistical tests were used: the Shapiro-Wilk test for data distribution evaluation and analysis of variance to compare age distribution according to different grades of eGFR (and Tukey's post hoc test, when necessary). In this analyses, confidence intervals of 95% and a significance level of 5% were used. Continuous quantitative variables were presented through central tendency and dispersion (mean±standard deviation) and qualitative variables through frequencies (absolute and relative). Significant associations were considered when p<0.05.

### RESULTS

A total of 280 indigenous participants were included: 184 (65.7%) from the Fulni-ô group and 96 (34.3%) from the Truká group, with a median age of 46 (interquartile range: 15.2) years in the entire cohort. According to the 2012 KDIGO criteria<sup>2</sup>, 59.9% of all participants had normal/high eGFR; 37.8% had mildly decreased excretory renal function (eGFR: 60–89 mL/min/1.73 m<sup>2</sup>); and 4.3% had substantially reduced eGFR (<60 mL/min/1.73 m<sup>2</sup>), which generally affected a higher age population (p<0.001) (Figure 2A).



Figure 2. Glomerular filtration rate stage (Chronic Kidney Disease Epidemiology Collaboration, without race correction) of the study population: (A) total population; (B) Fulni-ô; and (C) Truká.

In a more advanced degree of urbanization, the Truká people had a CKD prevalence of 6.2%, with no differences in kidney dysfunction across age groups. On the contrary, the Fulni-ô participants had a CKD prevalence of 3.3%, with a higher proportion of kidney dysfunction in older participants (of the six Fulni-ô indigenous people with CKD, five were older), when compared to young people from the same ethnicity (Figures 2B and 2C). In the prevalence of CKD between the two indigenous groups, no statistically significant difference was found (p=0.068) (Table 1). The Truká people presented a younger population with mildly to moderately decreased kidney function, with a median age of 47.5 years, contrasting with the median age of 63.5 years in the G3 Fulni-ô subgroup (Figures 2B and 2C).

The prevalence of hypertension and diabetes was 24.6 and 9.3%, respectively. Regarding the prevalence of hypertension, no association was found between the groups according to the eGFR. As for diabetes, the prevalence in the indigenous with an eGFR <60 mL/min/1.73 m<sup>2</sup> was 25% (3/12) compared to 8.6% (23/268) in the group with an eGFR ≥60 mL/min/1.73 m<sup>2</sup> (p=0.0453) (Table 1).

Notably, 95 (33.4%) individuals were classified as obese and 109 (38.9%) as overweight. No association was found between the prevalence of obesity in the groups according to estimated eGFR (p=0.327). However, among traditional risk factors for developing CKD, obesity was the only factor that showed a significant difference between the two indigenous groups, with a higher prevalence in the group with the highest degree of urbanization: 43.7% among the Truka (42/96) and 28.8% among the Fulni-ô (53/184) (p=0.0124) (Table 1).

# DISCUSSION

We identified a tendency of worse kidney function among the more urbanized Truka ethnicity when compared to the Fulni-ô people, suggesting that a more urbanized setting might be associated with worse kidney function. Additionally, our results also suggest that younger individuals are affected with intensity similar to the elderly among indigenous population with advanced urbanization levels.

The ELSA-Brazil cohort reported that 4.8% of the overall Brazilian population (n=14,636) had an eGFR below 60 mL/min/1.73 m<sup>2</sup>, compared to 7.2% of the 153 self-declared indigenous participants<sup>1</sup>. Socioeconomic disadvantages do not seem to fully explain the higher prevalence of CKD among indigenous participants in the ELSA study, as the entire cohort had stable employment and a high level of education. In accordance with our results, the ELSA study findings might, at least in part, be explained by the fact that the indigenous participants have experienced acculturation in a highly urbanized setting.

In non-indigenous Brazilian adults, the prevalence of systemic arterial hypertension is 21.4%<sup>13</sup>. In our study population, the prevalence of systemic arterial hypertension was slightly higher. However, this prevalence is slightly lower than in other ethnic groups that have been studied previously<sup>5,6</sup>. Other traditional risk factors related to CKD, such as diabetes mellitus and obesity, also showed considerable prevalence.

In relation to diabetes mellitus, according to a recently conducted survey<sup>14</sup>, the prevalence in the study groups was similar to that found in the Brazilian population and associated with CKD. This result may be closely linked to the high prevalence of obesity in this population, with an alarming prevalence of 33.4%. This number is higher than that found in a population-based survey conducted in Brazil (prevalence of 16.8% for men and 24.4% for women)<sup>15</sup>, and much higher than that found in the Brazilian Amazon Region, i.e., 14.4% in the Parkatêjê people and 15% in the Aruák people<sup>16</sup>. Among the risk factors for developing CKD, obesity was the only factor for which there was a statistical difference between the two indigenous groups.

Our results are likely due to the greater proximity and integration of the study groups with neighboring non-indigenous population and, consequently, the incorporation of an urban lifestyle. Consequently, changing dietary habits, especially the increased consumption of industrial foods, lead to an increase in chronic noncommunicable diseases and cardiovascular risk<sup>4,7</sup>. In this perspective study, it is likely that younger generations of indigenous people come in contact sooner and have more contact with these aspects of urban life than their ancestors.

Our study has limitations for generalizing the results due to the small sample size and its cross-sectional nature, which does not allow for the establishment of the causality of the association. Another limitation stems from the ethnic and cultural diversity of Brazilian indigenous people, which makes the final analysis difficult. Nevertheless, our results are relevant because they present unpublished data on a theme that has been less studied among Brazilian indigenous people. Furthermore, they suggest the influential role of urbanization in the prevalence of CKD and warn of its high prevalence in indigenous communities, which is a situation that occurs with indigenous people in other countries<sup>17</sup>. Finally, when considering the exclusion criteria of the PAI study (a study designed for a group of generally healthy participants), the low percentage of elderly in the sample (14.3%), the use of only GFR to estimate CKD, the percentage of indigenous people with CKD, and mildly decreased excretory renal function (G2) are significant and cause concern.

eGFR Ethnic group Variables Total eGFR <60 eGFR≥60 Fulni-ô Truká p-value p-value n=280 (100%) n=12 (4.3%) n=268 (95.7%) n=184 (65.7%) n=96 (34.3%) Ethnic group Fulni-ô 184 (65.7%) 6 (3.3%) 178 (96.7%) 0.389 Truká 96 (34.3%) 90 (93.8%) 6 (6.2%) Gender Female 182 (65%) 11 (6.1%) 171 (93.9%) 121 (65.7%) 61 (63.5%) 0.095 0.712° 97 (99.0%) Male 98 (35%) 1(1.0%)63 (34.3%) 35 (36.5%) Age (years) (Md; IQR) 46.0; 15.2 54.0; 12.5 45.5; 16.0 0.008<sup>d</sup> 46.0; 17 45.5; 9.2 0.791<sup>d</sup> 77 (27.5%) 0 (0.0%) 77 (100.0%) 55 (29.9%) 22 (22.9%) 30-39 years 0.015<sup>d</sup> 40-49 years 90 (32.1%) 3 (3.3%) 87 (96.7%) 52 (28.2%) 38 (39.6%) 0.051° 4 (5.5%) 28 (29.2%) 50-59 years 73 (26.1%) 69 (94.5%) 45 (24.5%) 60-70 years 40 (14.3%) 5 (12.5%) 35 (87.5%) 32 (17.4%) 8 (8.3%) Body mass index 0.761<sup>d</sup> 0.028<sup>d</sup> (Md; IQR) 27.5; 6.7 28.0; 2.2 27.3; 6.7 27.0; 6.2 29.3; 7.0 Low weight 1 (100.0%) 0 (0.0%) 1 (0.4%) 0(0.0%)1 (0.6%) Normal 75 (26.8%) 2 (2.6%) 73 (97.3%) 54 (29.4%) 21 (21.9%) Overweight 109 (38.9%) 8 (7.3%) 101 (92.7%) 76 (41.3%) 33 (34.4%) 0.442 0.238 Obesity I 68 (24.3%) 1(1.5%)67 (98.5%) 38 (20.6%) 30 (31.2%) Obesity II 18 (6.4%) 1 (5.5%) 17 (94.4%) 10 (5.4%) 8 (8.3%) Obesity III 9 (3.2%) 0 (0.0%) 9 (100.0%) 5 (2.7%) 4 (4.2%) 95 (33.4%) 93/268 (34.7%) 0.327 53 (28.8%) 42 (43.7%) 0.012 Obesity (I, I, II) 2/12 (16.7%) Presence of comorbidity No 184 (65.7%) 7 (3.8%) 178 (96.2%) 125 (67.9%) 59 (61.5%) 0.811° 0.278 84 (94.4%) 96 (34.3%) 5 (5.6%) 59 (32.1%) 37 (38.5%) Yes Type of comorbidity present 64 (92.8%) 41 (22.2% 28 (29.2%) 69 (24.6%) 5 (7.2%) 0.162 0.205° Hypertension 0.045 Diabetes 26 (9.3%) 3 (11.5%) 23 (88.5%) 20 (10.9%) 6 (6.3%) 0.206° Dyslipidemia 12 (4.3%) 0(0.0%)12 (100.0%) 0454 9 (4.9%) 3 (3.1%) 0.489° Smokinga 168 (79.6%) 5 (3.0%) 163 (97.0%) 149 (93.2%) 19 (37.2%) Active smoking Never smoked 0 12 (100.0%) 0.491 9 (5.6%) 3 (5.9%) < 0.001° 12 (5.7%) Stopped smoking 31 (14.7%) 2 (6.4%) 29 (94.6%) 2 (1.2%) 29 (56.8%) Alcoholismb 60 (95.2%) 29 (36.7%) Active drinking 63 (26.2%) 3 (4.8%) 34 (21.1%) Never drank 134 (55.9%) 5 (3.7%) 129 (96.3%) 0.532 101 (62.7%) 33 (41.8%) 0.015° Stopped drinking 43 (17.9%) 4 (9.3%) 39 (90.7%) 17 (21.5%) 26 (16.2) eGFR ≥90 mL/min/1.73 m<sup>2</sup> 100 62 60-89 mL/min/1.73 m<sup>2</sup> 78 28 0.068 <60 mL/min/1.73 m<sup>2</sup> 6 6

**Table 1.** Characterization of the study population, according to estimated glomerular filtration rate (estimated glomerular filtration rate <60 and</th> $\geq$ 60 mL/min/1.73 m²) and ethnic group (Fulni-ô and Truká indigenous people) (n=280).

<sup>a</sup>Assessed in 211 individuals. <sup>b</sup>Data from 240 individuals. <sup>c</sup>Chi-squared continuity correction. <sup>d</sup>Mann-Whitney U test. Md: median; IQR: interquartile range.

# CONCLUSION

A higher degree of urbanization seems to negatively influence the prevalence of kidney disease in Brazilian indigenous people, which is an important concern in assessing the youth in indigenous communities.

# **AUTHORS' CONTRIBUTIONS**

**OVG:** Conceptualization, Formal Analysis, Methodology, Writing – original draft, Writing – review & editing. **CDFS:** Conceptualization, Formal Analysis, Methodology, Software, Writing – original draft, Writing – review & editing. **ACA:** 

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Conceptualization, Formal Analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **MPG:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **JMN:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **LM:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **AMLS:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **JCMJ:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **MBN:** Project administration, Supervision, Visualization. **JACL:** Project administration, Supervision, Visualization.

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