**ORIGINAL ARTICLE**

# PREVALENCE AND FACTORS ASSOCIATED WITH CHRONIC KIDNEY DISEASE IN DIABETIC PATIENTS

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**Highlights:** (1). People with diabetes mellitus (DM) can develop CKD, with a 40% identification rate. (2). CKD has been associated with longer periods of diagnosis and treatment in diabetic individuals. (3). Actions for detecting and preventing CKD in diabetics are necessary within the SUS.

PRE-PROOF
(as accepted)
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## ABSTRACT

**Introduction:** The incidence of chronic kidney disease (CKD) has been increasing worldwide as a result of demographic and epidemiological transition processes, life expectancy, and the lack of control of chronic diseases, such as diabetes mellitus (DM). Thus, the present study aimed to evaluate the prevalence and factors associated with CKD in diabetic patients. **Method:** This was a cross-sectional study with diabetic patients enrolled in the Family Health Strategy (FHS), in the urban area of Rio Branco, state of Acre, in 2019. CKD was defined by GFR < 60 mL/1.72m², estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, or the presence of albuminuria > 29 mg/g. Measures of association were estimated by logistic regression, with a confidence level of 95%. **Results:** The prevalence of CKD was 40.0% in diabetic patients. A statistically significant association was found between CKD and treatment time longer than 10 years (1.74; 95%CI: 1.01; 3.02) and DM diagnosis (1.87; 95%CI: 1.05; 3.33) after adjustment. **Conclusion:** CKD has a high prevalence in diabetic patients, highlighting the need for public health measures for early detection and prevention of its progression.

**Keywords:** Chronic kidney disease. Diabetes mellitus. Associated factors. Prevalence.

## INTRODUCTION

The prevalence of diabetes mellitus (DM) has increased considerably throughout the world due to increased life expectancy, the adoption of an unhealthy lifestyle, a sedentary lifestyle, the growing prevalence of obesity, and the urbanization process[1]. Global estimates indicate that 382 million people lived with DM (8.3%), and this number could reach 592 million in 2035[2].

Uncontrolled blood glucose causes the development of serious and irreversible micro and macrovascular complications, including neuropathy, nephropathy, retinopathy, coronary disease, stroke, and peripheral vascular disease[1]. A meta-analysis study with data from 82 studies around the world showed a strong association between chronic kidney disease (CKD) and DM[3]; this relationship is well established in the literature[4].

CKD is considered one of the greatest global public health challenges, with 1.2 million deaths related to it worldwide and around 35 thousand in Brazil, with a mortality

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rate of 16.1/100,000 inhabitants, in 2017[5]. Among the reasons for death is the lack of access to renal replacement therapy[6].

The prevalence of CKD ranged from 45.1%, according to a North American cross-sectional study conducted with 2,915 diabetic patients using the MDRD equation[7], to 24.4% in Thailand, in a similar study with 1,096 diabetic patients using the CKD-Epi equation[8]. In Brazil, a survey of 7,457 patients aged ≥18 years detected a prevalence of 17.0% among diabetic patients according to the CKD-Epi equation[9]. According to a study involving 1,016 elderly people living in rural and urban areas of the municipality of Rio Branco (AC), the general prevalence of CKD was 21.4% and reached 41.5% in diabetic patients[10].

Research on CKD in diabetic patients should be encouraged to identify risk factors related to the onset of complications and point out ways to improve the prognosis of these patients. Early detection facilitates treatment and offers opportunities for therapeutic interventions to prevent or delay the onset of complications and improve results[11]. Given the above, intending to contribute to the development of actions and new health strategies aimed at early diagnosis of CKD and monitoring of DM patients, this study aimed to analyze the prevalence and factors associated with chronic kidney disease in diabetic patients in Rio Branco, state of Acre.

## MATERIAL AND METHODS

This was a cross-sectional study with individuals enrolled in the Family Health Strategy (FSH) diagnosed with DM in the urban area of Rio Branco (state of Acre) in 2019. The data are part of the matrix project entitled “Study of chronic diseases from the perspective of quality in health (Edoc-Quali)”, approved by the Research Ethics Committee of the Federal University of Acre under number 2.574.391. The present study complied with the provisions of CNS Resolution 466/2012, which deals with ethics in research involving human beings, and all participants signed the Informed Consent (IC).

The reference population for the study consisted of individuals aged 18 or over with type 2 DM, living in the urban area of Rio Branco, state of Acre, and enrolled in the FHS. Participants with cognitive disabilities that made it impossible to communicate or understand the questions in the interview, pregnant women, and patients with type 1 diabetes were excluded.

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Rio Branco relies on 68 Family Health Teams (FHTs) in the urban area, distributed throughout the two districts of the capital, allocated in 43 Primary Health Care Units. To calculate the sample size of users for this study, we considered a prevalence of 50.0% of changes in renal function, a margin of error of 3.5%, and a sampling design effect (SDE) estimate of 1.5, with a minimum sample of 308 diabetic patients. An additional 10.0% was added to cover any losses and refusals. The sample consisted of 324 diabetic patients. Due to the lack of information on albuminuria and creatinine, the final sample size in this study was 311 diabetic patients, which represents 2,372 individuals in the expanded sample.

All data collection procedures were carried out by trained personnel and supervised by the research coordination team. Data were collected by applying a general electronic, structured questionnaire in the health units of the selected FHTs. The sampling design was selected in two stages: unit and individual. In the first stage, 30 FHTs were drawn, and in the second, a draw of individuals with type 2 diabetes mellitus. Family registration forms were the source of information.

The individual form, structured with sociodemographic variables, health assessment, lifestyle habits, and the care process for people with DM. Physical and laboratory assessments were also carried out.

Anthropometric data included the measurement of weight, height and waist, hip, arm, and calf circumference, following the protocols recommended by the American College of Sports Medicine (ACSM) − all in duplicate, considering the measurement averages.

Weight was measured using a G-Tech® Bal Gl 200 digital scale accurate to 50 grams on a flat surface. Participants were instructed and were wearing light clothing with empty pockets and invited to step barefoot onto the center of the scale with their body upright, arms at their sides, and looking straight ahead.

Height was determined using a Sanny® portable stadiometer accurate to millimeters and the base on a flat surface. The participants, without using objects on their heads, remained placed with their backs to the device, with legs and feet parallel, weight distributed on both, arms sideways, and palms facing the body. After aligning the back of the head, back, buttocks, legs, and heels and the eyes facing forward using the Frankfurt plane for head positioning, the individual was asked to inhale deeply and hold their breath

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during the measurement, carried out by moving the mobile part of the stadiometer to the highest point of the head, compressing the hair enough to measure height.

Body mass index (BMI) resulted from the calculation of the ratio of weight (kg) to height (in meters squared: $m^2$). For analysis, participants were classified as underweight (< 18.5 $kg/m^2$), normal weight (from 18.5 to 24.9 $kg/m^2$), overweight (from 25 to 29.9 $kg/m^2$), and obese (≥ 30 $kg/m^2$).

Blood pressure (BP) was measured using a Beurer® automatic digital blood pressure monitor with an arm cuff, following the protocol recommended by the Brazilian Society of Cardiology. The final value was calculated by the arithmetic mean of the second and third measurements.

For the urine sample, approximately 50mL was obtained from the midstream of the first morning urine, collected in a duly identified sterile bottle, stored at a controlled temperature, and analyzed in a specialized laboratory. Samples were processed using physical-chemical and microscopic analysis of the sediment. A part was centrifuged, and the supernatant was taken for biochemical analysis of albuminuria levels using the method for the quantitative determination of albumin in human urine.

The peripheral blood sample was obtained by venipuncture in the antecubital fossa, with prior antisepsis. Biochemical analysis was carried out for triglycerides, total cholesterol and fractions (HDL − high-density lipoprotein and LDL − low-density lipoprotein), creatinine, and glycated hemoglobin were performed. After the results of the laboratory tests were made available and prior evaluation by the team, the tests were returned to the patients. In cases of altered results, the date for consultation with a health professional previously scheduled by the research team at the patient's reference health unit was indicated.

The dependent variable of the study was defined as chronic kidney disease identified by GFR < 60 mL/min/1.73$m^2$ and/or with the presence of albuminuria > 29 mg/g, using the CKD-Epi equation.

The independent variables selected were age group (up to 39 years, 40 to 59 years, and ≥ 60 years), sex (male and female), skin color (white and non-white), marital status (with a partner and without a partner), education (high school and over, elementary school, illiterate), smoking (smoker and non-smoker), alcohol consumption (yes and no).

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The practice of physical activity was assessed using the IPAQ questionnaire – International Physical Activity Questionnaire Short Version. Individuals who performed moderate-intensity physical activity for a minimum period of 30 minutes on five weekdays or vigorous-intensity aerobic physical activity for at least 20 minutes on three days of the week were classified as non-sedentary. Those who were considered sedentary were all those who did not meet this criterion.

Therapeutic adherence was analyzed using an instrument to assess attitudes toward taking medication (IAAFTR) composed of 10 structured questions with affirmative or negative answers. The proposed cutoff score is 7, with scores less than or equal to 7 referring to a negative attitude and scores higher than 7 referring to a positive attitude.

Adherence to treatment/knowledge about the disease was analyzed with the Batalla test composed of three questions to measure adherence based on the user's knowledge about their disease: Is DM and/or SAH a lifelong disease? Can DM and/or SAH be controlled with diet and/or medication? Name two or more organs affected by diabetes and/or hypertension.

Another variable assessed was eating habits (adequate nutrition or not) based on individuals' responses to the food frequency questionnaire. Individuals who consumed at least three times a week foods considered unsuitable for hypertensive and diabetic patients, such as pasta, chocolates, and butter, among others, were considered to have an improper diet. Also included were hours of sleep (11 hours or more, 6 to 10 hours, and 0 to 5 hours), comorbidities (yes or no), time since diagnosis of the disease (< 5 years, 6 to 10 years, and > 11 years), disease treatment time (< 5 years, 6 to 10 years, and > 11 years), complications (yes or no).

The laboratory variables analyzed were glycated hemoglobin to define diabetes control, yes for <7.0% or no for higher than or equal to 7.0%; total cholesterol (desirable < 190 mg/dL or high); HDL-cholesterol (desirable > 40 mg/dL or low); LDL-cholesterol (optimal < 100 mg/dL, desirable < 130 mg/dL, borderline > 130 mg/dL to 159 mg/dL and high/very high > 160 mg/dL); triglycerides (desirable < 150 mg/dL or high).

Body mass index (BMI) was classified as underweight (< 18.5 kg/m²); normal weight (from 18.5 to 24.9 kg/m²); overweight (from 25 to 29.9 kg/m²); and obese (≥ 30 kg/m²) (WHO, 2000). Independent variables were also considered: BP control,

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recommended by the Brazilian Society of Cardiology, diastolic blood pressure (DBP) < 90 mmHg, systolic blood pressure (SBP) <140 mmHg, current medications, participation in hypertensive and diabetic patient groups in the last 12 months (yes or no).

The accessibility and quality of the service were assessed by applying the Primary Care Assessment Tool (PCATool). For accessibility, the cutoff score is 7, with scores < 7 indicating no accessibility to services and > 7 with accessibility. To evaluate the quality of the service, scores ≥6.6 defined high or satisfactory quality, and values <6.6, considered poor or unsatisfactory, were used.

Data were analyzed in a descriptive and exploratory way to evaluate the distribution and characterize the studied population. Qualitative variables were described by absolute numbers and proportions. To test the differences between categorical variables, Pearson's chi-square test was adopted.

Bivariate analysis was carried out to explore the association between different variables and the outcome of chronic kidney disease. Regression models estimated the magnitude of association between the dependent variable and independent variables according to the proposed objectives. In the multiple analysis, those variables with a p-value less than 0.20 in the crude analysis were selected for inclusion, and the magnitude of the variables adjusted for age was evaluated. A significance level of $\alpha = 0.05$ was considered. Data analysis used the Complex samples routines of the Statistical Package for the Social Sciences (SPSS), version 20.0, for Windows.

## RESULTS

The prevalence of CKD in diabetic patients served by FHTs was 40.0%, using the CKD-EPI equation. According to the GFR < 60 mL/min/1.73 m², it was found in 14.0%, with 13.1% of individuals in stage 3, 0.6% in stage 4, and 0.5% in stage 5. Considering the prognosis of mild, moderate, and severe risk, the prevalence was 27.9%, 7.0%, and 5.1%, respectively. Albuminuria ≥ 30 mg/g was observed in 32.5% of diabetic patients (Table 1).

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**Table 1**. Prevalence by prognostic risk categories for CKD evolution according to GFR (CKD-EPI equation) and albuminuria in diabetic patients in Rio Branco, state of Acre, 2019.

* CKD-EPI = *Chronic Kidney Disease Epidemiology Collaboration* (mL/min/1.73m²). N = expanded n.

| Risk categories/ GFR (mL/min/m²) | Total* | | Albuminuria (mg/g) | | | | | | CKD (GFR* and/or albuminuria) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | A1 (< 30) | | A2 (30-299) | | A3 (≥ 300) | | | |
| | N | % | N | % | N | % | N | % | N | % |
| 1 ≥ 90 | 1,287 | 54.4 | 879 | 38.4 | 339 | 14.8 | 39 | 1.7 | 378 | 16.5 |
| 2 60-89 | 741 | 31.2 | 491 | 21.4 | 187 | 8.2 | 31 | 1.3 | 218 | 9.5 |
| 3a 45-59 | 207 | 8.7 | 111 | 4.9 | 45 | 2.0 | 33 | 1.4 | 189 | 8.3 |
| 3b 30-44 | 110 | 4.6 | 45 | 2.0 | 44 | 1.9 | 21 | 0.9 | 110 | 4.8 |
| 4 15-29 | 13 | 0.5 | 06 | 0.3 | 07 | 0.3 | 00 | 00 | 13 | 0.6 |
| 5 < 15 or dialysis | 14 | 0.6 | 07 | 0.3 | 00 | 00 | 00 | 00 | 0 7 | 0.3 |
| **Total** | **2,372** | **100.0** | **1.539** | **67.3** | **622** | **27.2** | **124** | **5.3** | **915** | **40.0** |

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The presence of CKD was higher among men, also in subjects aged 60 years or over, white skin color, those with less education, those without a partner, those who do not drink alcohol, smokers, and those who are sedentary (Table 2).

**Table 2**. Prevalence of CKD in diabetic patients according to sociodemographic characteristics and lifestyle habits in Rio Branco, state of Acre, 2019.

| Variables | Total | | CKD | | | | | | $OR_{crude}$ (95%CI) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Yes | | | No | | | | |
| | | | n | N | % | n | N | % | | |
| **Gender** | | | | | | | | | | 0,309 |
| Masculine | 117 | 898 | 49 | 387 | 43.1 | 68 | 511 | 56.9 | 1 | |
| Feminine | 199 | 1,526 | 75 | 576 | 37.7 | 124 | 950 | 62.3 | 0.80 (0.51;1.26) | |
| **Age group** | | | | | | | | | | |
| Up to 39 years old | 18 | 138 | 4 | 31 | 22.4 | 14 | 107 | 77.6 | 1 | |
| 40 to 59 years old | 121 | 905 | 36 | 262 | 28.9 | 85 | 643 | 71.1 | 1.41 (0.40;4.96) | 0.036 |
| ≥ 60 years | 177 | 1,381 | 84 | 670 | 48.5 | 93 | 711 | 51.5 | 3.28 (0.83; 2.90) | |
| **Skin color** | | | | | | | | | | 0.408 |
| White | 67 | 523 | 29 | 235 | 45.0 | 38 | 288 | 55.0 | 1 | |
| Non-white | 249 | 1,901 | 95 | 728 | 38.3 | 154 | 1,173 | 61.7 | 0.76 (0.38;1.50) | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Education** | | | | | | | | | | 0.148 |
| High school and over | 69 | 535 | 20 | 155 | 29.0 | 49 | 380 | 71.0 | 1 | |
| Elementary School | 195 | 1,472 | 82 | 629 | 42.7 | 113 | 843 | 57.3 | 1.82 (0.87;3.81) | |
| Illiterate | 52 | 417 | 22 | 179 | 43.0 | 30 | 238 | 57.0 | 1.84 (0.94;3.61) | |
| **Marital status*** | | | | | | | | | | 0.768 |
| With a partner | 61 | 460 | 24 | 175 | 38.1 | 37 | 285 | 61.9 | 1 | |
| Without a partner | 254 | 1,957 | 100 | 788 | 40.3 | 154 | 1,169 | 59.7 | 1.10 (0.57;2.12) | |
| **Alcohol consumption*** | | | | | | | | | | 0.886 |
| No | 296 | 2,271 | 116 | 902 | 39.7 | 180 | 1,369 | 60.3 | 1 | |
| Yes | 19 | 146 | 08 | 61 | 41.9 | 11 | 85 | 58.1 | 1.09 (0.30;4.06) | |
| **Smoking*** | | | | | | | | | | 0.042 |
| Non-smoker | 25 | 185 | 5 | 40 | 21.6 | 20 | 145 | 78.4 | 1 | |
| Smoker | 290 | 2,232 | 119 | 923 | 41.4 | 171 | 1,309 | 58.6 | 0.39 (0.15;0.99) | |
| **Physical activity*** | | | | | | | | | | 0.039 |
| Non-sedentary | 126 | 941 | 40 | 307 | 32.7 | 86 | 634 | 67.3 | 1 | |
| Sedentary | 189 | 1,486 | 84 | 665 | 44.4 | 105 | 821 | 55.6 | 1.65 (1.03;2.64) | |

N expanded based on the weights and the sampling design; % = proportion from N exp.; p-value = Pearson's Chi-square test. * Differences from the total are due to a lack of information in the variable.

According to clinical characteristics, the prevalence of CKD in diabetic patients indicated higher prevalence in individuals with comorbidities, hours of sleep between 6 and 10 hours, time since diagnosis and treatment of DM of 11 years or more, non-adherence to treatment/knowledge about the disease, with complications, no use of nephrotoxic medications, and a positive attitude toward taking medication. Furthermore, the prevalence was higher in patients with low HDL, borderline/high LDL, and high triglycerides. Taking DM control into account, in individuals who did not have control of the disease, the prevalence was 40.9%. Regarding the characteristics of the service, the prevalence was higher in subjects without accessibility and who had not participated in DM groups in the last 12 months but without significant differences comparing those with and without CKD (Table 3).

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**Table 3**. Prevalence of CKD in diabetic patients according to clinical characteristics and referring to the service in Rio Branco, state of Acre, 2019.

| Variables | Total | | CKD | | | | | | $OR_{crude}$ (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Yes | | | No | | | | |
| | n | N | n | N | % | n | N | % | | |
| **Sleep hours*** | | | | | | | | | | 0.314 |
| 11 or more | 17 | 86 | 06 | 40 | 34.5 | 11 | 46 | 65.5 | 1 | |
| 6 to 10 | 251 | 1,951 | 103 | 807 | 41.4 | 148 | 1,144 | 72.9 | 1.34 (0.45; 3.56) | |
| 0 to 5 | 42 | 312 | 12 | 93 | 29.9 | 30 | 219 | 70.1 | 0.81 (0.22; 2.99) | |
| **Comorbidities** | | | | | | | | | | 0.853 |
| No | 16 | 121 | 07 | 45 | 36.9 | 09 | 76 | 63.1 | 1 | |
| Yes | 300 | 2,903 | 117 | 918 | 39.9 | 183 | 1,985 | 60.1 | 1.13 (0.28; 4.56) | |
| **DM diagnosis time (years)*** | | | | | | | | | | 0.126 |
| < 5 | 137 | 1,055 | 48 | 365 | 34.6 | 89 | 690 | 65.4 | 1 | |
| 6 to 10 | 99 | 719 | 36 | 279 | 38.8 | 60 | 440 | 61.2 | 1.20 (0.63; 2.27) | |
| 11 or more | 78 | 684 | 38 | 304 | 49.7 | 40 | 380 | 50.3 | 1.87 (1.05; 3.31) | |
| **DM treatment time (years)*** | | | | | | | | | | 0.062 |
| < 5 | 142 | 1,093 | 49 | 374 | 34.2 | 93 | 719 | 65.8 | 1 | |
| 6 to 10 | 93 | 707 | 35 | 275 | 38.9 | 58 | 432 | 61.1 | 1.22 (0.68; 2.21) | |
| 11 or more | 74 | 573 | 37 | 294 | 51.2 | 37 | 279 | 48.8 | 2.02 (1.12; 3.66) | |
| **Adherence to treatment/knowledge about DM*** | | | | | | | | | | 0.413 |
| Yes | 152 | 1,125 | 57 | 420 | 373 | 95 | 705 | 62.7 | 1 | |
| No | 160 | 1,270 | 65 | 527 | 41.5 | 95 | 743 | 58.5 | 1.19 (0.77; 1.85) | |
| **Complications** | | | | | | | | | | |
| No | 191 | 1,458 | 72 | 566 | 38.9 | 119 | 892 | 61.1 | 1 | |
| Yes | 125 | 966 | 52 | 397 | 41.1 | 73 | 569 | 58.9 | 1.10 (0.64; 1.88) | 0.723 |
| **Nephrotoxic drugs** | | | | | | | | | | |
| No | 240 | 1,832 | 96 | 750 | 41.0 | 144 | 1,082 | 59.0 | 1 | |
| Yes | 76 | 591 | 28 | 212 | 35.9 | 48 | 379 | 64.1 | 0.81 (0.39; 1.69) | 0.549 |
| **Adequate nutrition** | | | | | | | | | | |
| Yes | 16 | 126 | 05 | 38 | 30.5 | 11 | 88 | 69.5 | 1 | |
| No | 299 | 2,292 | 119 | 925 | 40.3 | 180 | 1,367 | 59.7 | 1.54 (0.53; 4.50) | 0.401 |
| **Attitudes towards taking medication** (IAAFTR)* | | | | | | | | | | |
| Positive | 212 | 1,620 | 86 | 658 | 40.6 | 126 | 962 | 59.2 | 1 | |
| Negative | 94 | 730 | 35 | 279 | 38.2 | 59 | 451 | 61.8 | 0.90 (0.54; 1.50) | 0.678 |
| **Total cholesterol*** | | | | | | | | | | |
| Desirable | 148 | 1,142 | 60 | 454 | 40.1 | 88 | 688 | 59.9 | 1 | |
| High | 164 | 1,260 | 62 | 493 | 39.1 | 102 | 767 | 60.1 | 0.96 (0.56; 1.65) | 0.867 |
| **HDL cholesterol*** | | | | | | | | | | 0.067 |
| Desirable | 198 | 1,532 | 72 | 552 | 36.2 | 126 | 971 | 63.8 | 1 | |
| Low | 115 | 878 | 51 | 404 | 46.1 | 64 | 474 | 53.8 | 1.50 (0.97; 2.34) | |
| **LDL cholesterol*** | | | | | | | | | | 0.410 |
| Excellent | 108 | 845 | 43 | 337 | 39.9 | 65 | 508 | 60.1 | 1 | |
| Desirable | 90 | 664 | 31 | 229 | 34.4 | 59 | 435 | 65.9 | 0.79 (0.51; 1.23) | |
| Borderline | 64 | 509 | 27 | 223 | 43.8 | 37 | 286 | 56.2 | 1.18 (0.73; 1.88) | |
| High/very high | 34 | 273 | 11 | 85 | 31.0 | 25 | 188 | 69.0 | 0.68 (0.24; 1.88) | |
| **Triglyceride*** | | | | | | | | | | 0.085 |
| Desirable | 134 | 1,050 | 46 | 361 | 34.4 | 88 | 689 | 65.6 | 1 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| High | 179 | 692 | 77 | 595 | 44.0 | 102 | 756 | 56.0 | 1.50 (0.94; 2.41) | |
| **DM control*** | | | | | | | | | | 0.205 |
| Yes | 08 | 62 | 02 | 16 | 26.4 | 06 | 46 | 73.6 | 1 | |
| No | 290 | 2,216 | 116 | 906 | 40.9 | 174 | 1,310 | 59.1 | 1.53 (0.77; 3.05) | |
| **BMI (Kg/m²)*** | | | | | | | | | | 0.388 |
| < 24.9 | 01 | 08 | 01 | 08 | 100 | 00 | 00 | 00 | 1 | |
| 25 to 29.9 | 05 | 37 | 02 | 14 | 38.5 | 03 | 23 | 61.5 | 1.09 (0.52; 2.28) | |
| 30 and over | 290 | 2,229 | 111 | 862 | 38.7 | 179 | 1,367 | 61.3 | 0.89 (0.53; 1.48) | |
| **Access to the service** | | | | | | | | | | 0.977 |
| Yes | 165 | 1,282 | 67 | 508 | 39.7 | 98 | 774 | 60.3 | 1 | |
| No | 151 | 1,142 | 57 | 455 | 39.8 | 94 | 687 | 60.2 | 0.99 (0.63; 1.58) | |
| **Service quality*** | | | | | | | | | | 0.995 |
| Yes | 82 | 642 | 33 | 254 | 39.5 | 49 | 388 | 60.5 | 1 | |
| No | 231 | 1,762 | 89 | 696 | 39.5 | 142 | 1,066 | 60.5 | 0.99 (0.49; 2.05) | |
| **Participated in a DM group in the last 12 months*** | | | | | | | | | | 0.328 |
| Yes | 24 | 188 | 07 | 58 | 30.6 | 17 | 130 | 69.4 | 1 | |
| No | 290 | 2,219 | 116 | 896 | 40.4 | 174 | 1,323 | 59.6 | 1.53 (0.62; 3.79) | |

N expanded based on the weights and the sampling design; % = proportion from N exp.; p-value = Pearson's Chi-square test. * Differences from the total are due to a lack of information in the variable. HDL= High-density lipoprotein; LDL: Low-density lipoprotein BMI: Body mass index.

To evaluate the change in OR with the introduction of potentially confounding variables, a model was proposed with those variables with a p-value < 0.20 in the bivariate analysis, maintaining a p-value < 0.05 and with biological plausibility. After adjustments, variables age group, education, smoking, physical activity, HDL cholesterol, and triglycerides, which were selected because the p-value in the bivariate analysis was less than 0.20, showed no statistical significance. Diagnosis and treatment times of ≥11 years remained significant in the model, so having been diagnosed and being treated for DM for more than ten years increased the chance of having CKD, even after adjustment for potentially confounding variables (Table 4).

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**Table 4**. Description of factors associated with CKD in diabetic patients enrolled in the Family Health Strategy in Rio Branco, state of Acre, 2019.

| Variables | $OR_{adjusted}$ (95% CI) |
|---|---|
| **Age group (years)** | |
| Up to 39 | 1 |
| 40 to 59 | 1.15 (0.30; 4.38) |
| ≥ 60 | 2.59 (0.64; 10.48) |
| **Education** | |
| High school and over | 1 |
| Elementary School | 1.30 (0.67; 2.54) |
| Illiterate | 1.43 (0.64; 3.16) |
| **DM control** | |
| Yes | 1 |
| No | 1.59 (0.77; 3.26) |
| **Smoking** | |
| Non-smoker | 1 |
| Smoker | 0.43 (0.15; 1.25) |
| **Physical activity** | |
| Non-sedentary | 1 |
| Sedentary | 1.52 (0.93; 2.46) |
| **Triglycerides** | |
| Desirable | 1 |
| High | 1.50 (0.91; 2.48) |
| **HDL cholesterol** | |
| Desirable | 1 |
| High | 1.44 (0.93; 2.22) |
| **DM diagnosis time (years)** | |
| < 5 | 1 |
| 6 to 10 | 1.14 (0.61; 2.14) |
| 11 or more | 1.74 (1.01; 3.02) |
| **DM treatment time (years)** | |
| < 5 | 1 |

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| | |
|---|---|
| 6 to 10 | 1.13 (0.65; 1.97) |
| 11 or more | 1.87 (1.05; 3.33) |

OR: odds ratio adjusted for age.

## Discussion

The prevalence of CKD in diabetic patients was 40.0%, using the CKD-EPI equation, and was associated with the time of diagnosis and treatment of diabetes. Importantly, the prevalence of CKD in diabetic patients was higher than that identified in the Southeast of Brazil, with 243 individuals registered in HIPERDIA between May 2014 and August 2015, in which it was 20.2%, using the same criteria for defining CKD as in this research[12]. A previous study found that approximately 20.0-50.0% of individuals with type 2 diabetes may develop CKD[13].

In São Paulo, research carried out at a university hospital identified a 32.1% prevalence of diabetes in chronic kidney disease patients[14]. In Australia, a study involving 90,550 individuals over the age of 18 with type 2 diabetes mellitus found that 8.9% had CKD, while 7.3% did not have the disease, despite the clinical condition compatible with this diagnosis[15].

Regarding the stages of CKD, according to the GFR, 16.5% of the sample were in stage 1, 9.5% in stage 2, 8.3% in stage 3a, 4.8% in stage 3b, 0.8% in stage 4, and 0.3% in stage 5. In India, a survey of 117 diabetic individuals revealed a prevalence of 45.3%, similar to that found here. The proportion of patients was 13.75% in stage 1, 41% in stage 2, 6.8% in stage 3a, 26.5% in stage 3b, and 12% in stage 4; there were no patients classified as stage 5[16]. In Spain, the prevalence of CKD in type 2 diabetic patients was 27.9%, a lower value than observed in Rio Branco, Acre, with 3.5% in stages 1, 6.4% in stage 2, 16.8% in stage 3, and 1.2% in stages 4 and 5[17].

In Northeastern Brazil, an investigation evaluating the factors associated with the glomerular filtration rate in 143 patients with DM2 revealed that renal function deficit occurred in 7.0%, which presented a GFR < 60 mL/min/1.73 m². In just over half, the GFR was slightly reduced, given that 51.4% of individuals were classified in stage 2[18]. The data differ from our findings as they present higher prevalence in the early stages of CKD and lower in more advanced stages since 16.5% were in stages 3 to 5 in Rio Branco.

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Patients with CKD in stages 1 to 3 (GFR > 30mL/min/1.73 m²) generally do not present evident clinical manifestations and are asymptomatic. The prevalence of CKD in type 2 diabetic patients is three times higher than in the non-diabetic population. The prevention of diabetic nephropathy is essential, as is the strict control of blood glucose and BP levels, the reduction of proteinuria, and the inhibition of the renin-angiotensin system to prevent or delay CKD[16].

Among the factors associated with CKD, a higher prevalence was found with increasing age, although not statistically significant. This relationship is very well documented in the literature. In general, there is a decrease in renal function after 30 years of age (even in healthy individuals), with a decline in GFR by 1 mL/min/1.73 m² per year, resulting in a higher number of people with CKD in the older age groups[16,18]. In Barcelona, in a sample of 97,655 individuals aged 60 years or over, a positive association was reported in the multivariate analysis between GFR and age[19], a fact not observed in the present study.

Regarding lifestyle habits, in the bivariate analysis regarding physical activity, the prevalence was 44.4% in sedentary individuals and 32.7% in non-sedentary individuals but without significance after adjustment. In Japan, an analysis carried out on 120 patients with CKD showed reduced physical function as the disease progressed. The study showed that a sedentary lifestyle increases by 2.14 times the risk of kidney disease[20].

Exercise through physical activity is an important tool in the treatment of chronic diseases, including CKD, as it reduces cardiovascular risks and inflammatory processes while leading to better BP control, increased strength, cardiorespiratory fitness, and physical function[21]. Still considering lifestyle habits, the proportion of CKD in diabetic patients was higher in the group of smokers (41.4%) than in the group of non-smokers (21.6%). Smoking is intrinsically associated with the progression of kidney damage in patients with diabetic nephropathy or not and is an independent risk factor for kidney function, as it has vasoconstrictive, thromboembolic, and direct effects on the endothelium. Therefore, this habit should be discouraged[18].

As for changes in the lipid profile, total cholesterol was elevated at 39.1%, HDL-c was low (46.1%), LDL-c was elevated (31%), and triglycerides were elevated (44%), not remaining significant in the multiple analysis. In a study carried out in Northeastern

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Brazil, LDL-c was increased in 76.7% of patients, followed by a decrease in HDL-c in 61%, an increase in total cholesterol (47.3%), and an increase in triglycerides (40.4%)[18,22].

In the present study, in the bivariate analysis, despite not showing statistical significance, a higher proportion of CKD was found in the group of illiterate individuals, followed by elementary school and high school and over, with a prevalence of 43.0%, 42.7%, and 29.0%, respectively. In a sample of 9,720 participants in Australia, a lower risk of cardiovascular outcomes, as well as CKD progression, was reported in patients with a higher educational level[23]. A systematic review in 2015 concluded that lower levels of education are a negative predictive factor for the health of kidney patients[24]. As one of the components related to socioeconomic factors, education plays a key role in the development of CKD due to the difficulty in accessing health services to identify its onset and evolution, as well as the lack of knowledge about its progression factors[25].

The lack of association between the analyzed variables and CKD in diabetic patients in the present study should be seen with caution given that, in the literature, this information was widely researched and achieved statistical significance. Perhaps the lack of significance was due to the sample size or the chosen study design.

The longer time of diagnosis and treatment showed statistical significance after adjustment, which points to the long-term and continuous effect of diabetes on kidney function. A cohort study in the USA with veterans with newly diagnosed DM2 found a prevalence of CKD in stages 1 to 5 of 31.6%, with half classified as stages 3 or over[26]. The moment of onset of DM2 is difficult to determine; however, the influence of DM on the onset of CKD is evident in this study.

The development of CKD in diabetic patients is a consequence of permanent hyperglycemia that produces metabolic and hemodynamic changes, being a relevant but not crucial factor in the development of glomerular damage. There are several mechanisms for the occurrence of these injuries, including activation of the sympathetic nervous system, sodium retention, and negative regulation of the natriuretic peptide system. Such changes can be found early without a reduction in GFR[27]. In order to maintain normal blood glucose levels, hyperinsulinemia occurs, a condition that also contributes to renal fibrosis, by inducing the growth of mesangial cells, inhibiting apoptosis and reducing the activity of matrix metalloproteins[28,29].

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As a limitation of the present study, the study design prevents causal inference, which means that associations must be evaluated with caution; therefore, it cannot be said whether they are the causes or consequences of CKD. Nevertheless, it is worth highlighting that the exploratory analysis of factors is extremely important and a fundamental tool for the early diagnosis of the disease.

Another limitation is the specific diagnosis of CKD based on a blood and urine sample to calculate GFR and albuminuria since the diagnosis is confirmed by the persistence of the condition for more than three months. A single measurement of GFR may not reflect an accurate scenario, as patients with acute renal failure may have been included as chronic kidney patients. In order to control errors in estimating GFR, the performance of laboratory tests in the same laboratory was standardized, and its estimation was made based on serum creatinine using the CKD-EPI equation.

The scarcity of Brazilian studies on the detection of CKD and associated factors in hypertensive and diabetic patients is highlighted; therefore, the present study is unprecedented in the population of Rio Branco. Also, it brought important clarifications, presenting the stages of CKD based on the definition proposed by KDIGO (2013)[30] and the prognostic risks, which contributes to comparisons with international and national studies. Most national studies used self-report or were conducted with patients on dialysis therapy or were based on GFR or proteinuria. In the case of the present research, both criteria were used to define CKD, which reduces the chance of errors. Population-based studies should be carried out in all regions of Brazil to evaluate regional differences and thus better understand the factors related to the onset or progression of CKD.

## CONCLUSION

The prevalence of CKD among diabetic patients was high; the time of diagnosis and treatment were factors associated with kidney damage. These patients with changes in renal function require follow-up through periodic examinations and referral to specialized services. This follow-up is essential for early detection and delaying the progression of the disease through routine consultations and exams. Furthermore, promoting awareness and better knowledge about the topic among health professionals is an extremely important factor in improving monitoring in public health systems.

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