**ORIGINAL ARTICLE**

# 24-HOUR URINARY SODIUM EXCRETION AND ASSOCIATED FACTORS IN NON-DIALYSIS CHRONIC KIDNEY DISEASE

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**Highlights:** (1) 24-hour urinary excretion, the gold standard method, should be incorporated into clinical. (2) Stage II Chronic Kidney Disease with higher median sodium excretion. (3) Obesity was a risk factor for developing CKD.



http://dx.doi.org/10.21527/2176-7114.2025.50.14297

How to cite:
Teixeira TCS, Dias RSC, Brito DJ de A, França AKT da C, Dantas ACF de A, Diniz JS, Campelo RLC. et al. 24-hour urinary sodium excretion and associated factors in non-dialysis chronic kidney disease. Rev. Contexto & Saúde, 2025;25(50): e14297

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**24-HOUR URINARY SODIUM EXCRETION AND ASSOCIATED FACTORS IN NON-DIALYSIS CHRONIC KIDNEY DISEASE**


## ABSTRACT

This study aims to determine urinary sodium excretion in 24-hour urine and correlate it with associated factors in patients with non-dialysis chronic kidney disease. **Methodology:** Cross-sectional study with 116 individuals. Demographic, nutritional, clinical and laboratory data were evaluated. Urinary sodium excretion was analyzed in 24-hour urine and glomerular filtration rate was estimated using the CKD-EPI equation. Categorical variables were presented as frequencies and percentages, numerical mean ± SD or median. Normality was tested using the Shapiro Wilk test. The median was used to determine urinary sodium excretion in the stages of Chronic Kidney Disease. Pearson's correlation was used to verify the association of the variables with 24-hour urinary sodium excretion. **Results:** Mean age 51.1 ± 14.0 years, 75.9% female, hypertensive and diabetic 54.3% and 19.8% respectively, 60.9% were in stage one of Chronic Kidney Disease. The median 24-hour urinary sodium excretion by disease stage was higher in stages II 118.6 mmol/L/24h (78.4-155.5) and I 117 mmol/L/24h (96.6-141.0). They correlated positively with 24-hour urinary sodium excretion, body mass index ($r = 0.19$; p-value 0.004), urinary creatinine ($r = 0.48$; p-value <0.001), and negatively with age ($r = -0.26$; p-value 0.006) and total cholesterol ($r = -0.20$; p-value 0.036). There was a predominance of women, hypertensive patients, stage I chronic kidney disease, elementary school, and income below the minimum wage. **Conclusion:** Age and total cholesterol were negatively correlated with urinary sodium, while body mass index and urinary creatinine were positively correlated.


**Keywords:** Sodium. Renal Elimination. Chronic Kidney Disease. Glomerular Filtration Rate.

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## INTRODUCTION

For a long time, the adverse effects associated with high salt intake were only related to blood pressure[1], since researchers had already demonstrated a positive linear correlation between the prevalence of hypertension and sodium intake[2].

Currently, several other effects have been reported, and high sodium consumption has become considered one of the main risk factors for developing diseases such as stroke, left ventricular hypertrophy and Chronic Kidney Disease (CKD), regardless the additive effects of salt on Blood Pressure (BP)[3].

Changes in body sodium intake and content are detected through changes in effective arterial blood volume and its effect on pressure-sensitive receptors in the vascular wall, renal afferent arteriole and heart. The activation of these receptors leads to changes in renal effector systems, such as the renin-angiotensin II-aldosterone axis (SRAA), the sympathetic nervous system and the release of vasopressin and Atrial Natriuretic Peptide[4].

Systemic arterial hypertension (SAH) represents one of the major public health problems in developing countries and in the world, and is the main cause of chronic kidney disease in Brazil[5].

CKD is a clinical syndrome secondary to definitive alterations in renal function and/or structure, characterized by its slow, progressive and irreversible evolution[6]. Considered a public health problem, financially expensive, with high morbidity and mortality and that has an impact on the quality of life of the population[7].

It is estimated that, in the world, 9.1% of the population, which corresponds to about 700 million people, have some stage of CDR[8]. In Brazil, the number of individuals with CKD is not known precisely due to late diagnosis and underreporting[9].

The two main causes of CKD in Brazil are SAH and Diabetes Mellitus (DM)[5]. Both are relevant and influence their progression, interfering with glomerular filtration, proteinuria and reduced response to SRAA block[4].

There has been a consensus that excessive salt consumption is associated with multiple adverse health outcomes, including a positive causal relationship with blood pressure[10].

According to the World Health Organization (WHO, 2013)[11], consumption of more than 5 grams of sodium chloride (NaCl) per day increases the prevalence of hypertension and consequently the risk of cardiovascular disease and kidney disease. Given the above, several countries have instituted public policies, encouraging the reduction of daily salt consumption

by the population.

Therefore, this study has as guiding questions:

a) Do non-dialytic chronic kidney patients show higher levels of sodium excretion?

b) Are demographic, lifestyle, clinical laboratory and nutritional factors associated with higher levels of sodium excretion in this population?

Considering that there are few Brazilian studies evaluating salt consumption in the general population and especially in individuals with CKD, and that there are divergences regarding the amount of salt consumed, and that high sodium consumption has deleterious effects on health.

Therefore, the urinary excretion of sodium for 24 hours is the best way to evaluate the consumption of this mineral. Thus, 24-hour urine collection is widely considered as the gold standard method for intake assessment, and it is often used as a measure to compare and validate other methods of sodium intake evaluation[12]. Therefore, the objective of this article is to determine urinary sodium excretion in urine for 24 hours and correlate with associated factors in patients with chronic non-dialytic kidney disease.

## METHOD

Cross-sectional study with individuals accompanied in the outpatient clinics of the Center for the Prevention of Renal Diseases, in stages I, II, 3A, 3B of CKD with glomerular filtration rate between 90-30mL/min/1.73m$^2$, aged 18 years or older, followed by a nephrologist. Individuals with chronic consumptive diseases (cancer, HIV), pregnant women, urinary infection, autoimmune diseases and use of loop diuretic were not included in the study.

The sample size was calculated considering an average excretion of 203.1mmol/L/24h, standard deviation of 84.9 mmol/L/24h and a sampling error of 8mmol/L/24h[4], totaling 116 individuals.

The selected individuals were informed of the study object, and those who agreed to participate signed the informed consent form. They answered a questionnaire regarding demographic, socioeconomic and lifestyle information and were guided about the process of collecting laboratory tests and anthropometric evaluation.

The income was measured in minimum wages corresponding to the value of the year of study (1,045 BRL) and schooling was measured in years of study, without schooling (0 year), elementary school (1-4 years), average (5-8 years) superior (> 8 years). The collection was previously scheduled coinciding with the day of consultation with nephrologist.

Urinary sodium assays were made in urine sample of 24 hours and urine sample isolated. Individuals were instructed to begin collecting the material one day before delivery. When they woke up, emptied the bladder and marked the time in which they began collecting. From then on, all urine produced was stored in a suitable container and packaged under refrigeration until the 24h of collection. Urine samples with a volume of less than 400 ml were disregarded due to the possibility of error in collection. The isolated urine samples were collected at the site of delivery of the material.

The laboratory assays of interest were: fasting blood glucose, total cholesterol, LDL-c, HDL-c, triglycerides, serum and urinary albumin, serum and urinary creatinine, serum sodium and urinary summary of urine: The tests were processed in the Clinical Analysis Laboratory of the Presidente Dutra University Hospital of the Federal University of Maranhão (HUPD-UFMA).

Blood glucose values were considered altered in the range of (100 - 125mg/dL) according to the American Diabetes Association (ADA)[13]. Dyslipidemia was categorized as (1) isolated hypercholesterolemia: isolated LDL elevation (≥160 mg/dL); (2) isolated hypertriglyceridemia: isolated triglyceride elevation (≥150 mg/dL); (3) mixed hyperlipidemia: LDL ≥160 mg/dL and triglycerides ≥150 mg/dL; and (4) Low HDL: <40 mg/dL in men and <50 mg/dL in women[14].

Renal function was evaluated by serum creatinine and glomerular filtration (GF) estimation, based on the equation described below.

$$Equation\ CKD-EPI\ (LEVEY\ et\ al.,2009)$$

$$GF\left(\frac{\frac{mL}{min}}{1{,}73}m^2\right) = 141 \times min\left(serum\frac{creatinine}{\kappa},1\right)\alpha \times max\left(serum\frac{creatine}{\kappa},\right)$$

$$-1{,}209 \times 0{,}993Age \times 1{,}018\ if\ women - 1{,}159\ if\ black$$

For the diagnosis of reduced renal function, a Glomerular Filtration Rate (GFR) 60mL/min/1.73 $m^2$ was considered. For diagnostic confirmation of altered renal function, individuals with GFR ≤60mL/min/1.73 $m^2$ were submitted to the new dosage three months after the first[15].

The anthropometric evaluation was performed by means of body weight, height and waist circumference (WC). The weight was measured with a calibrated scale (Filizola®, Brazil)

with a maximum capacity of 150 kg and subdivisions every 100 g and height, with the aid of a portable stadiometer (Alturexata®, Brazil) with a scale from 0 to 220 cm and accuracy of 0.1 cm.

The WC was measured at the midpoint between the last rib and the iliac crest at the time of expiration, using non-extendable anthropometric trellis (Sanny®, Brazil) and the adopted cut-off point was classified according to WHO (1997)[16], high risk when WC ≥94 cm for men, ≥80 cm for women; very high risk, WC ≥102 cm for men, ≥88 cm for women.

The nutritional status was also evaluated according to body mass index, obtained by the ratio between body weight and height square, and adopted the classification proposed by the World Health Organization[16], being considered for adults: low weight when BMI < 18,5 kg/m$^2$; eutrophication, BMI ≥ 18.5 kg/m$^2$ and < 25 kg/m$^2$ overweight, BMI ≥ 25 kg/m$^2$ and < 30 kg/m$^2$; and obesity, BMI ≥ 30 kg/m$^2$. In the elderly, the adopted cut points were: < 22 kg/m 2, low weight; ≥ 22 and < 27 kg/m$^2$, eutrophication; ≥ 27 kg/m$^2$ overweight[17].

The categorical variables were presented by means of frequencies and percentages; the numerical ones by mean ± SD (standard deviation). The normality of variables was tested by the Shapiro Wilk test. The median was used to determine urinary sodium excretion in different stages of CKD. To verify the association of variables that correlated with urinary excretion of sodium for 24 hours, the Pearson or Spearman correlation was used, as indicated. The significance level adopted was 5%. The software used was STATA 14.0.

This study was approved by the Research Ethics Committee of the University Hospital of the Federal University of Maranhão (CEP-HUUFMA), according to the attributions defined in the CNS Resolution n. 466/2012 and Operational Standard no. 001 of 2013 of the CNS. Opinion Number: N. 2.904.987.

## RESULTS

There were 116 individuals evaluated, the mean age was 51.1 14.0 years, female predominance (75.9%). There was a higher frequency of individuals with elementary school (65.2%), with family income lower than the minimum wage (42.7%). The prevalence of smoking and alcohol consumption were 3.4% and 26.7%, respectively. They reported not practicing physical activity 54.3% of the individuals. The hypertensive and diabetic individuals accounted for 54.3% and 19.8%, respectively. The majority of patients were in stage 1 of chronic kidney disease (60.9%) (Table 1).

**Table 1.** Distribution of sociodemographic, lifestyle and clinical variables of individuals monitored at the Kidney Disease Prevention Center of the University Hospital of the Federal University of Maranhão, São Luís, Maranhão, 2021.

| Variables | n | % (95% CI) |
|---|---|---|
| **Sex** | | |
| Male | 28 | 24.1 (16.7-33.0) |
| Female | 88 | 75.9 (67.0-83.3) |
| **Schooling** | | |
| ≤ 9 years | 39 | 34.8 (26.1-44.4) |
| >9 years | 73 | 65.2 (55.6-73.9) |
| **Income** | | |
| < 1MW | 49 | 42.7 (33.4-52.2) |
| ≥1 ≤ 2 | 46 | 40.0 (31.0-49.6) |
| >2 MW | 20 | 17.4 (10.9-25.6) |
| **Smoking** | | |
| Yes | 4 | 3.4 (0.9-8.6) |
| No\|quit | 112 | 96.6 (91.4-99.0) |
| **Alcohol consumption** | | |
| Yes | 31 | 26.7 (18.9-35.7) |
| No\|quit | | 73.3 (64.3-81.1) |
| **Physical activity** | | |
| Yes | 53 | 45.7 (36.4-55.2) |
| No | 63 | 54.3 (44.8-63.6) |
| **SAH** | | |
| Yes | 63 | 54.3 (44.8-63.6) |
| No | 53 | 45.7 (36.4-55.2) |
| **DM** | | |
| Yes | 23 | 19.8 (13.0-28.2) |
| No | 93 | 80.2 (71.7-87.0) |
| **CKD stages** | | |
| 1 | 70 | 60.9 (51.3-69.8) |
| 2 | 39 | 33.9 (25.3-43.3) |
| 3[a] | 4 | 3.5 (0.9-8.7) |
| 3b | 2 | 1.7 (0.2-6.1) |

MW = minimum wage in BRL; SAH = systemic arterial hypertension; DM = diabetes mellitus; CKD = chronic kidney disease, CI = Confidence Interval.

Regarding 24-hour urinary sodium excretion by CKD stages, higher median values were observed in stage II 118.6 mmol/L/24h (78.4-155.5) and in stage I 117 mmol/L/24h (96.6-141.0). However, there was no statistically significant difference (p-value 0.213) (Table 2).

**Table 2.** Distribution of 24-h urinary sodium excretion by CKD stages of individuals followed at the Kidney Disease Prevention Center of the University Hospital of the Federal University of Maranhão, São Luís, Maranhão, 2021.

| Variable | CKD | | | | *p*-value |
|---|---|---|---|---|---|
| **24h Na** | **Stage 1** | **Stage 2** | **Stage 3a** | **Stage 3b** | |
| Md (P25-P75 mmol/L/24h) | 117 (96.6-141.0) | 118.6 (78.4-155.5) | 85 (70.8-100.9) | 74.2 (67.7-80.6) | 0.213 |

Data presented in Md (P25-P75); CKD = chronic kidney disease. Kruskal-Wallis test

A positive correlation was observed with 24h urinary sodium excretion: BMI (r = 0.19; p-value 0.004), urinary creatinine (r = 0.48; p-value <0.001) and negative age (r = -0.26; p-value 0.006), total cholesterol (r = -0.20; p-value 0.036) (Table 3).

**Table 3.** Correlation of 24-hour urinary sodium excretion with sociodemographic, nutritional, clinical and laboratory variables of individuals monitored at the Kidney Disease Prevention Center of the University Hospital of the Federal University of Maranhão, São Luís, Maranhão, 2021.

| Variables | Urinary Na mmol/L/24h | |
|---|---|---|
| | r | *p*-value |
| **Age** | -0.26 | 0.006 |
| **BMI** | 0.19 | 0.004 |
| **WC** | 0.09 | 0.326 |
| **eGFR** | 0.17 | 0.083 |
| **Serum Cr** | -0,04 | 0.672 |
| **Urinary Cr** | 0,48 | <0.001 |
| **Serum albumin** | 0,02 | 0.865 |
| **Urinary albumin** | 0,17 | 0.073 |
| **CT** | -0.20 | 0.036 |
| **LDL** | -0.18 | 0.062 |
| **HDL** | -0.12 | 0.223 |
| **TG** | -0.09 | 0.340 |
| **DM** | 0.11 | 0.240 |

24h Na = 24h urinary sodium; r = Peason's variable correlation; BMI = body mass index; WC = waist circumference; eGFR = estimated glomerular filtration rate; Serum Cr = serum creatinine; Urinary Cr = urinary creatinine; TC = cholesterol; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TG = triglycerides; DM = diabetes mellitus.



## DISCUSSION

A higher percentage of women was observed. It is well established in the literature that women have a higher prevalence of CKD when compared to men; however, the incidence of patients with terminal kidney disease is 1.5 times higher in men than in women[15].

The survey conducted in the American population showed that 7.78% of adult women versus 5.77% of men had CKD in the early stages, but men exhibited higher prevalence of CKD in stage 5 (0.07% of women and 0.15% of men). These data confirm that there are more men in the most advanced stages[18].

It is believed that women seek more health care and consequently have greater access to disease diagnoses[19].

In relation to the Chronic Noncommunicable Diseases (CNCDs), in this study, there was a higher prevalence of individuals with SAH. It is known that this represents the first cause of CKD in Brazil[5]. Studies on the importance of hypertension in CKD demonstrate its

deleterious effect due to increased glomerular injury, whose damage causes microvascular lesions, renal vasoconstriction, loss of peritubular capillaries, local ischemia, among others, causing glomerular filtration decline[20].

In our findings, diabetes mellitus presented a lower percentage compared to SAH, however, it requires attention because it is the second largest cause of CKD in Brazil and the first in the world, becoming an independent risk factor for which doubles in patients with an albumin/creatinine ratio > 30 mg/g, highlighting the importance of adequate treatment to prevent microvascular lesion[6].

Regarding the average age, the results obtained are in accordance with the distribution of the census carried out in 2020 by the Brazilian Society of Nephrology (SBN), which indicates that patients aged 45 to 64 years are the most affected. Since, from the age of 40 years, anatomical and physiological alterations of the kidneys occur and renal function tends to decrease naturally with advancing age[21]. These factors associated with unbalanced eating habits and non-physical activity result in CNCDs, which are known to be a major public health problem[22].

The largest number of individuals were in stage I of the CKD, which requires attention because, despite being a relatively young population, it needs periodic monitoring through consultations and exams[22]. Results of the KNOW-CKD study found that the highest quartile of urinary excretion of 24-hour Na was associated with the risk of compound renal outcome in a multivariate risk model. Confirming that urinary sodium excretion is a predictor of CKD progression[23].

It is noteworthy that Primary Care plays an important role in the longitudinal monitoring of CKD and CNCDs through promotion and surveillance actions in health[25].

The evolution of CKD to stage V burdens the Unified Health System. Study conducted in the UK by Elshahat et al. (2020)[26] demonstrated that the advancement of CKD implies higher public spending, both from the point of view of the health system and society, contributing to lower quality of life related to health, as well as lower patient life expectancy.

Regarding the level of education of patients, most had elementary school and income less than a minimum wage. Low socioeconomic levels contribute substantially to the development of CKD, as they tend to generate vulnerability, since this population has less access to health and preventive examinations, with consequent late medical diagnosis[19].

A high percentage of the sample did not perform physical activity. Physical activity is considered a protective factor of other diseases that accelerate or trigger CKD such as obesity,

dyslipidemia, SAH and DM. In addition, it has been recommended as an important non-pharmacological treatment for improvement in glomerular filtration levels, psychological factors, cognitive factors and quality of life[27].

The recommendations of the Kdigo state that physical activity in individuals with CKD should be encouraged and they should be accompanied by a specialized professional, performing at least 150 minutes per week, at a level compatible with their cardiovascular and physical health, taking into account age and the presence of other comorbidities[6].

As for sodium excretion, stage II of CKD expressed higher median excretion compared to stage III. Exceeding the recommended by the World Health Organization, demonstrating non-adherence to low dietary intake as recommended by WHO[11]. The lower values expressed in stage III may be justified by the fact that these individuals have multidisciplinary outpatient clinical follow-up. Since, in patients with non-dialytic CKD, reducing salt intake from the earliest stages is important to prevent complications throughout the course of the disease.

An essay published by Molina *et al.* (2018)[28] confirmed that sodium consumption is strongly linked to blood pressure, in which individuals who consume more than 2 g/day are prone to increased blood pressure.

Moreover, high sodium consumption is associated with the progression of CKD. Deficiencies in sodium excretion are often associated with impaired renal function, since the kidneys cannot eliminate sodium and consequently there is an increase in blood pressure and proteinuria, glomerular hyperfiltration and reduced response to the intrarrenal Renin-Angiotensin System (RAS) blocking[4].

Urinary sodium excretion was positively correlated with BMI and urinary creatinine. The high BMI influences the development of CKD by causing hemodynamic, structural and histological renal alterations, as well as metabolic and biochemical disorders that predispose to kidney disease, even if the renal function is normal in conventional tests, and are also associated with cardiovascular diseases[29].

The latest census conducted by the Brazilian National Health Survey found that six out of ten Brazilians have excess weight 61.7%, 26.8% of these were obese[30]. These data correspond to a significant increase of individuals who are overweight that is a proven factor for the development of CNCDs, among them CKD, it is known that obesity is an independent risk condition for CKD[31].

In view of this, obesity causes an increase in the body metabolic demand, compromising the proper functioning of the kidneys that runs with glomerular hypertension associated with

increased renal plasma flow, filtration fraction, of sodium resorption and glomerular filtration rate and leads to progressive loss of renal function. In addition, eating patterns of obese people have been cited as possible risk factors for CKD[32].

Thus, the prevention and treatment of obesity represent the main way to primary, secondary and delayed prevention of the disease through lifestyle changes such as regular practice of physical activity and balanced eating[33].

Urinary creatinine is widely used in clinical practice to calculate the clearance of creatinine that provides an indicator of GFR. For the most part, creatinine is eliminated from the blood entirely by the kidneys, and its decrease in urinary clearance results in increased blood creatinine and consequent renal dysfunctions[34].

Another initial evaluation method for the identification of renal injury using urinary creatinine is the albumin/creatinine ratio, which consists of one of the main laboratory markers of kidney parenchymal lesion, through the detection of microalbuminura[34].

Although it is a relatively late marker for the detection of CKD in patients in the early stages, since creatinine only increases when renal function is already significantly impaired. In addition, its concentration depends not only on kidney function but also on diet and muscle mass, which varies according to sex, age and ethnicity. However, it is noticed that this marker is still widely used in clinical practice due to low cust[35].

The present study found a negative correlation between urinary excretion of sodium with age and total cholesterol. It is agreed in the literature that age should be considered as a criterion for renal function, since kidney functionality decreases over time. In addition, hypertension and diabetes mellitus are recognized as the main risk factors for CKD[4].

Individuals with CKD have biochemical and physiological changes that cause an imbalance in the lipid profile, and these changes can occur at all stages of the disease36. High cholesterol levels lead to the formation of plaques of atheromas in the walls of arterial vessels and these plates undergo ruptures and generate crystals that lodge in small renal arterioles, forming emboli crystals that cause narrowing of the lumen of the arterioles, which result in progressive renal alterations, also increasing the risk of heart attack or stroke encephalico[37].

Our study has some limitations: 1) since it is a cross-sectional study, it is not possible to establish a causal relationship. 2) since it was developed in a single research center, it does not allow generalization to the population of CKD carriers.

As strengths of this study, the use of a gold standard marker to estimate sodium consumption is highlighted. Demonstrating that 24-hour urine collection remains the best

method of evaluating dietary sodium intake for accurate measurement of intake in the population.

## CONCLUSION

The study identified a higher median sodium excretion in stage II of CKD. Age and total cholesterol were negatively correlated with urinary sodium excretion. BMI and urinary creatinine had positive correlation. Obesity was a risk factor for the development of CKD.

High sodium intake was observed in this population, above the recommended level. These findings suggest that the measurement of urinary sodium excretion, especially in 24h urine, as a gold standard method, should be incorporated into clinical practice as a measure to prevent disease, especially renal and cardiovascular in this population that is already known to be more predisposed to these diseases.

These findings confirm the importance of multiprofessional monitoring, especially of nurses and nutritionists who perform an important role in patient awareness, acting in health promotion and prevention, as caregivers and educators, who reflect in improvement of the quality of life.

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Submitted: April 11, 2023

Accepted: July 16, 2024

Published: February 17, 2025

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All authors approved the final version of the manuscript.

Conflict of Interest: There is no conflict of interest.

**24-HOUR URINARY SODIUM EXCRETION AND ASSOCIATED FACTORS IN NON-DIALYSIS CHRONIC KIDNEY DISEASE**

**Funding:** Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão – FAPEMA.

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