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Original Article

Health Profile And Risk Of Sarcopenia In Patients With Chronic Kidney Disease On Hemodialysis In The Agreste Region Of Alagoas.

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Running Title : Health Profile and Risk of Sarcopenia in Patients with Chronic Kidney Disease.

Abstract

Introduction: The health profile of patients with chronic kidney disease (CKD) undergoing hemodialysis reflects the interaction between social and uremic factors. With the nutritional transition, sarcopenia has become an increasingly common finding in hemodialysis centers. Objective: To assess the health profile and risk of sarcopenia in CKD patients undergoing hemodialysis in the Agreste region of Alagoas, Brazil.
Methods: A cross-sectional study was conducted with hemodialysis patients of both sexes, aged ≥18 years. Socioeconomic, clinical, and anthropometric data were collected after the dialysis session. Sarcopenia risk was estimated using the SARC-F questionnaire. Laboratory data were extracted from medical records.
Results: Among the 300 participants, 58.3% were at risk of sarcopenia. The majority were female (50.7%), comprised of older people (55.7%), and individuals who self-identify as Black people (59.3%). In univariate analysis, a history of hospitalization was associated with a higher risk of sarcopenia (OR = 1.63; p = 0.05). Statistical modeling indicated a higher likelihood of risk in patients with underweight arm circumference (OR = 1.97; p = 0.01), low body mass index (OR = 1.76; p = 0.04), and iron supplementation (OR = 2.02; p < 0.01).
Conclusion: The risk of sarcopenia is high among hemodialysis patients in the Agreste region of Alagoas, particularly in those with nutritional deficits and undergoing iron supplementation.

Keywords : Musculoskeletal System; Health Vulnerability; Undernutrition.

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INTRODUCTION

Chronic Kidney Disease (CKD) poses a high risk of morbidity and mortality and imposes significant costs on public health, as it can progress silently to advanced stages[1]. According to the Brazilian Society of Nephrology, Brazil has 886 active hemodialysis units, corresponding to a national average of 4.3 dialysis centers per million population (pmp). The lowest rates were observed in the Northeast region (3.0 pmp), with 84% of these units operating under public funding[2]. The same survey reported an increase in the prevalence of overweight and obesity among dialysis patients, reaching 46% of the total, consistent with the national trend.

The decline in kidney function is associated with reduced resting energy expenditure, which, combined with decreased food intake, may lead to an adaptive metabolic slowdown as a protective mechanism against significant body weight loss. This condition can also trigger subclinical inflammation, which increases energy expenditure. In this context, monitoring risk conditions is essential[3].

Furthermore, common conditions among hemodialysis patients,such as the use of β-blockers, hyperparathyroidism, changes in hydration status, and the accumulation of uremic toxins,contribute to a chronic inflammatory state characterized by increased release of pro-inflammatory cytokines. Several biomarkers are involved in this process, including parathyroid hormone, high-sensitivity C-reactive protein, adipokines such as leptin and adiponectin, and myokines such as irisin. Together, these factors affect energy expenditure and intensify muscle protein catabolism, increasing the risk of sarcopenia even in individuals with excess weight[4,5].

Sarcopenia is defined as the loss of muscle mass and strength, accompanied by impaired physical performance. Although it is commonly associated with aging, its prevalence in CKD can reach up to 19%, becoming more evident as the disease progresses[6]. Several factors contribute to the decline in the clinical status of these patients, including disturbances in protein and energy metabolism, biochemical and hormonal changes, and inadequate food intake, often resulting from nausea and vomiting,common manifestations of uremic toxicity[5].

One study sought to identify dialysis centers in Brazil that routinely assessed and treated sarcopenia. Only 37% (n=23) routinely evaluated sarcopenia, and of these, 11.3% were located in the Northeast region. The most widely used guideline to define the condition was EWGSOP2, emphasizing handgrip strength measurement and bioelectrical impedance analysis. The most frequent interventions included nutritional counseling and physical exercise[7].

The EWGSOP2 guideline recommends using the SARC-F questionnaire for screening patients with signs of sarcopenia. This tool consists of five items assessing strength-related limitations and is a low-cost, easily applicable method for identifying the risk of sarcopenia (RS), although it shows low to moderate sensitivity and specificity in predicting low muscle strength[8]. Despite being a prevalent condition, particularly among socioeconomically vulnerable individuals, and strongly associated with clinical complications, higher hospitalization rates, dependency, and mortality, there is a scarcity of studies addressing sarcopenia in the hemodialysis population in the Agreste region of Alagoas[9,10].

The Agreste region of Alagoas is characterized by low socioeconomic indicators, income inequality, low educational attainment, and limited access to healthcare services. A large portion of the population lives in vulnerable conditions, especially in rural areas, which contributes to poorer health outcomes. These conditions foster the development of chronic diseases and nutritional disorders[9]. Therefore, given the gaps in the literature, it is essential to investigate the prevalence and factors associated with sarcopenia in hemodialysis patients in the Agreste region of Alagoas.

METHODS

The study was conducted in accordance with Resolutions 466/12 and 510/16 of the Brazilian National Health Council[11,12]. The Research Ethics Committee of the Federal University of Alagoas, Brazil, approved the protocol (CAAE No. 61726822.2.0000.5013; approval number 5,704,399).

All participants signed the Informed Consent Form

This was an observational, analytical, cross-sectional study. Data collection was conducted in the hemodialysis services of Santa Rita Regional Hospital and Manoel André Hospital Center, located in the municipalities of Palmeira dos Índios and Arapiraca, respectively. Data collection was carried out between January and April 2023 and included clinical and biochemical information obtained from medical records, the application of a standardized socioeconomic questionnaire developed by the research group, anthropometric assessment, and the Simplified Questionnaire for Rapid Diagnosis of Sarcopenia with scoring (SARC-CalF). Recruitment was performed through direct invitation to patients in the hemodialysis units. At the time of invitation, the project was presented, and each step of the research was explained.

Patients with chronic kidney disease undergoing hemodialysis, of both sexes, aged 18 years or older, and on renal replacement therapy for at least six months were included. Exclusion criteria were individuals diagnosed with neoplasms in the past five years, patients with non-dialytic chronic kidney disease, pregnant women, and those with a history of hospitalization for sepsis, major surgery in the last six months, or high HIV viral load.

Sociodemographic variables included sex (male and female), age [adult (18–59 years) and elderly (≥ 60 years)], race [other races (White, Asian, Indigenous) and Black (Black, Brown)], education (> 8 and ≤ 8 years of schooling), and family income (> 1 and ≤ 1 minimum wage). Data were also collected on the presence of other chronic non-communicable diseases (NCDs) (diabetes, glomerulopathy, and hypertension), history of hospitalization (none and yes), iron supplementation (none and yes), and use of erythropoietin (none and yes).

For anthropometric assessment, weight was measured using a digital scale (capacity of 180 kg) and height with a portable stadiometer (up to 200 cm). Participants wore light clothing, without accessories or shoes, and were instructed to maintain an upright position[13]. Body Mass Index (BMI) was calculated using post-hemodialysis weight and height (kg/m²), adopting the World Health Organization (1995) cut-off points for adults,normal weight (18.5–24.9), underweight (< 18.5), and overweight (≥ 25.0),and those of Lipschitz (1994) for the elderly,normal weight (22–27), underweight (< 22), and overweight (> 27)[14].

Arm circumference (AC) and calf circumference (CC) were also measured. AC was measured with the arm flexed at 90° and analyzed by percentiles[15,16], using the Blackburn and Thornton[17] classification: normal (90–110%), malnutrition (< 90%), and overweight (> 110%). CC was measured on the left leg using a non-extensible, flexible tape (Cescorf/1–200 cm) at the largest point between the ankle and knee, with the leg relaxed. Adequate CC was considered ≥ 34 cm for men and ≥ 33 cm for women[18].

Biochemical variables included hemoglobin (Hb), serum potassium, serum phosphorus, dialysis adequacy index (Kt/V), and urea reduction ratio (URR), using the following reference values: Hb 10–12 g/dL; potassium 4.0–6.0 mmol/L; serum phosphorus 3.5–5.5 mg/dL; Kt/V ≥ 1.2 per session; URR≥ 65% per session[19,20].

After data collection, the information was entered into Microsoft Excel spreadsheets and reviewed by two independent evaluators to ensure compliance and database integrity. The spreadsheet was then exported and processed using SPSS software, version [21].

Absolute and relative frequencies were calculated for categorical variables, and measures of central tendency and dispersion for continuous numerical variables, considering the assumption of normality assessed by the Kolmogorov-Smirnov test with Lilliefors correction.

Associations between categorical variables were assessed using Pearson's Chi-square test, and the magnitude of association was expressed as the odds ratio (OR) with the corresponding 95% confidence interval. Comparison of central tendency measures was performed using the Mann-Whitney test, respecting the assumptions of non-parametric distribution.

To verify the modeling of associations, logistic regression analysis was performed, adjusted for sex (dichotomous), age (continuous), and income (continuous), using the backward elimination strategy. Variables with p-values < 0.20 in univariate analyses were retained in the regression model.

A significance level of 5% was adopted for all tests.

RESULTS

The sample comprised 300 participants, of whom 200 were from Manoel André Hospital Center and 100 from Santa Rita Regional Hospital.

As shown in **Table 1**, the prevalence of sarcopenia risk (SR) was 58.3% (n = 175). Most participants were female (n = 152; 50.7%), aged 60 years or older (n = 167; 55.7%), and self-identified as Black (n = 172; 59.3%). Low educational attainment was observed in 59.3% (n = 172), and 42.7% (n = 128) reported a family income below the minimum wage.

Approximately 69% of the sample (n = 206) had a diagnosis of diabetes, with a higher frequency in the SR group (n = 120; 68.6%). Regarding clinical variables, 60.7% (n = 187) were receiving iron supplementation, and 63.7% (n = 191) were using erythropoietin. Patients with a history of hospitalization had a 1.63-fold higher risk of SR (CI: 0.98–2.71; p = 0.05), while iron supplementation was associated with a 1.97-fold higher risk (CI: 1.23–3.16; p < 0.01) (**Table 1**).

Table 1. Distribution and Univariate Analysis of Sociodemographic Variables and Clinical Aspects of the Population from the Agreste Region of Alagoas Under Dialysis Support, According to the Presence of Sarcopenia Risk.

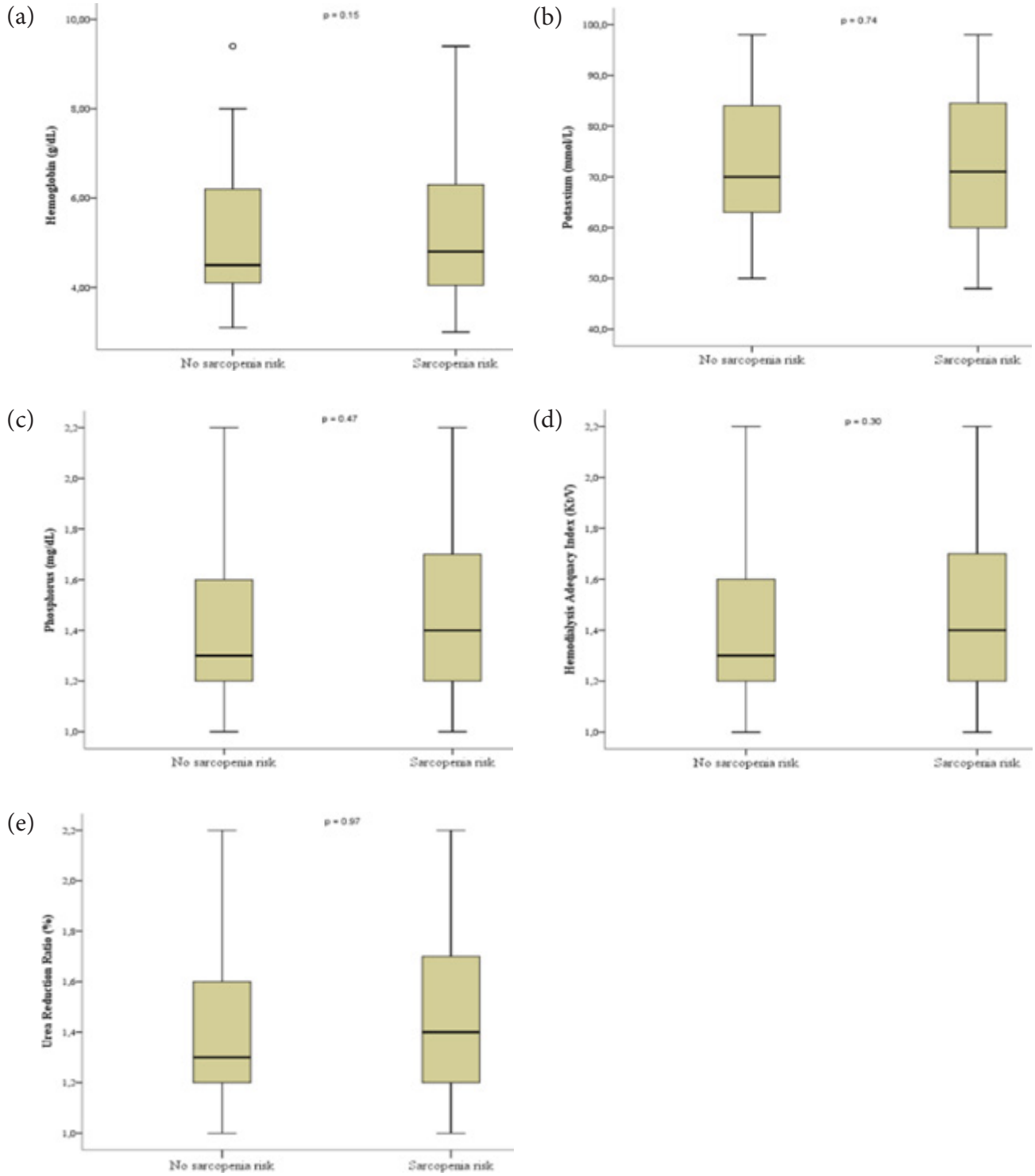
Variables	Total	No Sarcopenia risk	Sarcopenia risk	p	OR (CI)
	N = 300 100%	N = 125 41.7%	N = 175 58.3%		
	n (%)	n (%)	n (%)		
Sociodemographic					
Sex					
Male	148 (49.3)	66 (52.8)	82 (46.9)	0.31	1.26 (0.80–2.00)
Female	152 (50.7)	59 (47.2)	93 (53.1)		
Age					
Adult	133 (44.3)	62 (49.6)	71 (40.6)	0.12	1.44 (0.90–2.28)
Older people	167 (55.7)	63 (50.4)	104 (59.4)		
Race					
Other racial groups	144 (48.0)	56 (44.8)	88 (50.3)	0.34	0.80 (0.50–1.27)
Black people	156 (52.0)	69 (55.2)	87 (49.7)		
Education					
> 8 years	122 (40.7)	45 (36.0)	77 (44.0)	0.16	0.71 (0.44–1.14)
≤ 8 years	178 (59.3)	80 (64.0)	98 (56.0)		
Family income					
> 1 Minimum wage	172 (57.3)	67 (53.6)	105 (60.0)	0.26	0.77 (0.48–1.22)
≤ 1 Minimum wage	128 (42.7)	58 (46.4)	70 (40.0)		
Health condition					
Other chronic diseases a					
Diabetes	206 (68.7)	86 (68.8)	120 (68.6)	0.96	0.98 (0.60–1.62)
Glomerulopathy	48 (16.0)	21 (16.8)	27 (15.4)	0.74	0.90 (0.48–1.68)
Hypertension	192 (64.0)	75 (60.0)	117 (66.9)	0.22	1.34 (0.83–2.16)
Hospitalization history					
No history	205 (68.3)	93 (74.4)	112 (64.0)	0.05	1.63 (0.98–2.71)
With history	95 (31.7)	32 (25.6)	63 (36.0)		
Iron supplementation					
No supplementation	118 (39.3)	61 (48.8)	57 (32.6)	< 0.01	1.97 (1.23–3.16)
With supplementation	182 (60.7)	64 (51.2)	118 (67.4)		
Erythropoietin					
No use	191 (63.7)	75 (60.0)	116 (66.3)	0.26	0.76 (0.47–1.22)
In use	109 (36.3)	50 (40.0)	59 (33.7)		

Source: Authors, 2025. a Sum of frequencies of conditions does not total the sample size with chronic disease, as individuals may have more than one. Analyses considered exclusively the presence/absence of the specific condition.

A statistically significant association was found between arm circumference (AC) and SR ($p < 0.01$), with low weight observed in 66.9% (n = 117) of this group. Regarding BMI, 48.0% (n = 84) of individuals with SR were classified as normal weight, and 35.4% (n = 62) as underweight. Calf circumference (CC) and AC showed no association with the outcome.

Comparison of hemoglobin, potassium, and phosphorus levels showed no differences between groups with and without SR (**Figure 1**). The same was observed for dialysis adequacy indicators and urea reduction ratio (**Table 2**).

Figure 1. Comparison of serum hemoglobin, potassium, and phosphorus levels, and hemodialysis adequacy markers, according to the presence of sarcopenia risk.



Source: Authors. Legend: (a) Hemoglobin (b) Potassium (c) Phosphorus (d) Hemodialysis Adequacy Index (e) Urea Reduction Ratio.

Table 2. Characterization and Association Analysis Between Anthropometric Assessment and Laboratory Tests of the Population from the Agreste Region of Alagoas Under Dialysis Support, According to the Presence of Sarcopenia Risk.

Variables	Total	No Sarcopenia risk	Sarcopenia risk	p	OR (CI)
	N = 300 100%	N = 125 41.7%	N = 175 58.3%		
	n (%)	n (%)	n (%)		
Anthropometry					
AC Adequate Underweight Overweight	 96 (32.0) 180 (60.0) 24 (8.0)	 47 (37.6) 63 (50.4) 15 (12.0)	 49 (28.0) 117 (66.9) 9 (5.1)	 < 0.01	 ***
WC Adequate Inadequate	 227 (75.7) 73 (24.3)	 92 (73.6) 33 (26.4)	 135 (77.1) 40 (22.9)	 0.48	 0.82 (0.48–1.40)
CC Adequate Inadequate	 110 (36.7) 190 (63.3)	 49 (39.2) 76 (60.8)	 61 (34.9) 114 (65.1)	 0.44	 1.20 (0.74–1.93)
BMI Normal weight Underweight Overweight	 156 (52.0) 93 (31.0) 51 (17.0)	 72 (57.6) 31 (24.8) 22 (17.6)	 84 (48.0) 62 (35.4) 29 (16.6)	 0.13	 ***
Laboratory tests					
Hemoglobin No anemia With anemia	 124 (41.3) 176 (58.7)	 58 (46.4) 67 (53.6)	 66 (37.7) 109 (62.3)	 0.13	 1.43 (0.89–2.27)
Potassium Adequate Inadequate	 147 (49.0) 153 (51.0)	 63 (50.4) 62 (49.6)	 84 (48.0) 91 (52.0)	 0.68	 1.10 (0.69–1.74)
Phosphorus Adequate Inadequate	 189 (63.0) 111 (37.0)	 82 (65.6) 43 (34.4)	 107 (61.1) 68 (38.9)	 0.43	 1.21 (0.75–1.95)
Kt/V Adequate Inadequate	 238 (79.3) 62 (20.7)	 101 (80.8) 24 (19.2)	 137 (78.3) 38 (21.7)	 0.59	 1.16 (0.65–2.06)
URR Adequate Inadequate	 168 (56.0) 132 (44.0)	 67 (53.6) 58 (46.4)	 101 (57.7) 74 (42.3)	 0.47	 0.84 (0.53–1.34)

Source: Authors, 2025. Legend: BMI – Body Mass Index; CC – Calf Circumference; WC – Waist Circumference; Kt/V – Hemodialysis Adequacy Index; URR – Urea Reduction Ratio. ***Computed only for a 2×2 table. [a]Normality classification of parameters: Hemoglobin 10–12 g/dL; Potassium 4.0–6.0 mmol/L; Phosphorus 3.5–5.5 mg/dL; Kt/V ≥ 1.2 minimum per session; URR ≥ 65% per session. Values below indicate inadequacy[19,20].

In the adjusted logistic regression, iron supplementation was associated with a higher likelihood of SR (OR = 2.02; p < 0.01). Low weight, as assessed by arm circumference (OR = 1.97; p = 0.01) and BMI (OR = 1.76; p = 0.04), was also significantly associated with the outcome (**Table 3**).

Table 3. Multivariable Logistic Regression Analysis to Identify Factors Associated with the Diagnosis of Sarcopenia Risk in the Population from the Agreste Region of Alagoas Under Dialysis Support.

Variables	OR	95% CI	Adjusted p-value
Iron supplementation	2.02	1.00–3.11	< 0.01
Low AC	1.97	1.15–3.38	0.01
Low BMI	1.76	1.24–3.31	0.04

Source: Authors. Legend: p adjusted for sex, age, and family income.

DISCUSSION

This study investigated the health profile and sarcopenia risk in patients with chronic kidney disease on hemodialysis in the Agreste region of Alagoas, revealing a high frequency of SR (58.3%) in a population predominantly composed of elderly, Black individuals with low income and educational attainment. Analyses showed a significant association between SR and markers of body composition (underweight) and nutritional status (iron supplementation), which remained independent risk factors. Although laboratory variables did not show significant associations with SR, a high prevalence of anemia was observed in the SR group. These findings underscore the complex interaction between nutritional status, clinical condition, and sarcopenia risk in hemodialysis patients, highlighting the need for integrated care strategies, particularly in socioeconomically vulnerable settings.

The SR prevalence observed in this study (58.3%) is striking and considerably exceeds percentages reported in other hemodialysis populations. In Southern Brazil, for example, preliminary studies have reported prevalence rates ranging from 12% to 37%[21,22]. Internationally, sarcopenia prevalence in hemodialysis patients reaches up to 40%[23]. The figure found here also surpasses that observed in another municipality within the same state. In Maceió, the state capital, Theodosio et al.[24] reported prevalence rates of 20% using SARC-F and 32.6% using SARC-CalF among hemodialysis patients. Similarly, Amaral et al.[25] reported prevalence rates of 44% and 37% among those with CKD undergoing conservative treatment and hemodialysis, respectively. These data suggest that patients in the Agreste region may be exposed to more unfavorable clinical and social conditions, potentially contributing to increased sarcopenia risk. Methodological differences, such as diagnostic criteria and regional contexts, may account for variations across studies. Nevertheless, the high prevalence observed in this work reinforces the need for systematic sarcopenia screening in the CKD context, particularly among highly vulnerable populations.

The sample's demographic composition, with a predominance of females, elderly individuals, and those with low income and education, reflects a common profile in Northeastern Brazil[26]. National studies indicate that advancing age and low socioeconomic status are key factors for worsening nutritional status and increasing SR in renal patients[22,27]. Reviews suggest that demographic characteristics, inflammatory processes, and comorbidities are associated with muscle loss in CKD[28]. Low education and income limit access to adequate nutrition and self-care, increasing the risk of malnutrition and muscle disuse[29]. Physiologically, women have less muscle mass than men, increasing vulnerability to muscle loss. With aging, muscle protein synthesis and the anabolic response decrease. These changes can promote inflammation and impair mitochondrial function in muscles, raising sarcopenia risk[30]. However, no significant association with these variables was found in the studied population.

High rates of hypertension and diabetes were observed in the sample, but no statistical association with SR was found. Conversely, univariate analysis indicated that individuals with a history of hospitalization had a 1.63-fold higher odds of SR ($p = 0.05$), suggesting a trend between functional decline and more severe clinical events. Similarly, iron supplementation was significantly associated with SR. Cohort studies have confirmed higher hospitalization rates for intermediate or intensive care in renal patients, associated with sarcopenia, diabetes, and hypertension, to support cardiovascular events and correct anemia[31–33]. Consistently, Guedes et al. linked iron deficiency to poorer quality of life and mortality risk[34].

Iron deficiency affects one-third of CKD patients. When manifested as anemia, it is a strong marker of disease severity. Proper management helps delay renal dysfunction and cardiovascular complications[35]. When untreated, anemia can progress to chronic muscle hypoxia, leading to symptomatic muscle changes. In addition, metabolic dysfunctions, malnutrition, and physical inactivity—common in CKD—favor the development of uremic myopathy, a condition strongly associated with sarcopenia[35,36]. Approximately 36% of participants had anemia and SR; however, unlike reports in the literature, no association between these two conditions was found, indicating the need for further studies investigating their concomitant manifestation in CKD patients with greater specificity.

BMI profiling indicated a predominantly normal-weight population, followed by undernutrition and, to a lesser extent, overweight. This result differs from several studies and may represent an additional risk for the population in Alagoas, as obesity tends to be more prevalent and is considered a protective factor in this clinical group[24,25]. Clinical deterioration and high mortality rates are more common among normal-weight and malnourished renal patients[37]. Regarding anthropometry, CC is understood as a sensitive marker of muscle composition, and although low CC was frequent in more than half of participants, low AC was the only measure significantly associated with SR. This discrepancy may be related to individual factors or measurement limitations, underscoring the importance of using multiple indicators in anthropometric assessment of dialysis patients[38,39].

In multivariate regression, iron supplementation (OR = 2.02; $p < 0.01$) and low AC (OR = 1.97; $p = 0.01$) remained significantly associated with sarcopenia risk. In this analysis model, low BMI (OR = 1.76; $p = 0.04$) was also related to SR. Iron supplementation may indicate chronic nutritional deficiency and inflammation, as the response to erythropoietin depends on the body's functional state[36]. The absence of an association with anemia reinforces the need for hematimetric and muscle

mass evaluations as previously discussed. Regarding AC, previous studies indicate that adequate AC is associated with lower mortality in CKD patients, reinforcing its relevance as a clinical-nutritional indicator[38]. Finally, despite its limitations in describing body composition, low BMI remains an important predictor of sarcopenia in the hemodialysis population, as reported in a meta-analysis by Yifei Zhang et al.[40]. According to these authors, dialysis patients who are older, have lower BMI, lower muscle mass index, and diabetes are more likely to develop sarcopenia.

The variables associated with sarcopenia risk in CKD patients on dialysis reflect more severe clinical conditions and nutritional depletion, reinforcing the need for interventions aimed at correcting major risk factors.

This study has limitations, including its cross-sectional design, which precludes causal inferences. The absence of robust diagnostic tools for sarcopenia limited comparisons between different screening measures. The scarcity of biochemical tests available in dialysis clinics prevented a deeper analysis of metabolic and inflammatory markers. Furthermore, the sample, comprising both adults and older adults without specific age stratification, may have introduced variability in factors associated with sarcopenia risk.

CONCLUSION

This study identified a high prevalence of sarcopenia risk among chronic kidney disease patients undergoing hemodialysis in the Agreste region of Alagoas, primarily among those classified as underweight, as evidenced by both BMI and arm circumference. The association between sarcopenia risk, iron supplementation, and hospitalization suggests the role of nutritional and inflammatory factors in muscle health within this population. Although many patients were classified as eutrophic by BMI, complementary measures such as calf circumference revealed signs of depletion, highlighting the limitations of BMI as a standalone indicator. These findings reinforce the importance of more comprehensive nutritional assessments, including functional and body composition indicators, as well as the development of public health policies aimed at preventing sarcopenia in socially vulnerable contexts, such as the population studied, characterized by low education, reduced income, and belonging to racially marginalized groups.

Authors' Contributions

All authors have read and approved the final version of the manuscript, meeting the authorship criteria established by the International Committee of Medical Journal Editors (ICMJE) (http://www.icmje.org/recommendations/).

- Study conception and design: Andreza Ferreira da Silva; Jessiane Rejane Lima Santos; Samir Buainain Kassar; Juliana Célia de Farias Santos.
- Data acquisition, analysis, and interpretation: Andreza Ferreira da Silva; Jessiane Rejane Lima Santos; Samir Buainain Kassar; Juliana Célia de Farias Santos.
- Manuscript drafting or critical revision for important intellectual content: Andreza Ferreira da Silva; Jessiane Rejane Lima Santos; Müller Ribeiro-Andrade; Juliana Célia de Farias Santos.
- Final approval for publication: Andreza Ferreira da Silva; Jessiane Rejane Lima Santos; Müller Ribeiro-Andrade; Juliana Célia de Farias Santos.

Conflict of Interest

The authors declare no conflict of interest regarding participants or collaborators involved in the project. They affirm that their work adhered to the principles of protecting participants' rights and safety, in accordance with Resolutions No. 466/2012 and No. 510/2016 of the Brazilian National Health Council.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to ethical and privacy restrictions but may be obtained from the corresponding author upon reasonable request.

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