# Malnutrition and cardiovascular risk in haemodialysis patients with chronic kidney disease

## *Desnutrição e risco cardiovascular em pacientes com doença renal crônica em hemodiálise*

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**A B S T R A C T**

**Objective**

To verify the association between nutritional status and traditional and non-traditional cardiovascular risk factors in haemodialysis patients.

**Methods**

A cross-sectional study with 132 patients over 18 years of age on haemodialysis to evaluate nutritional status through Subjective Global Assessment. Information on traditional and non-traditional cardiovascular disease

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risk factors were obtained using a structured questionnaire; the Framingham score was also used to assess cardiovascular risk. Data analysis was performed using the Chi-square Test or Fischer Exact Test and a Log-binomial Regression Model.

**Results**

Malnutrition affected 31.1% of patients. Among them, a higher percentage of smokers (*p*=0.016), former smokers (*p*=0.034) and diabetes *Mellitus* patients (*p*=0.001) were detected. Malnutrition was found to be 4.53 times more prevalent in diabetic individuals (95%CI: 1.99-10.27) and 2.26 times more prevalent among former smokers (95%CI: 1.04-4.95). Malnourished individuals exhibited a 4.03 times prevalence of moderate to severe cardiovascular risk.

**Conclusion**

A high prevalence of malnutrition and of other risk factors for cardiovascular disease were observed. Such factors included diabetes *Mellitus*, smoking and former smoker conditions and were associated with malnutrition. In addition, it was found that malnourished individuals were more likely to develop cardiovascular disease within 10 years.

**Keywords**: Cardiovascular diseases. Chronic kidney disease. Haemodialysis. Malnutrition.

## R E S U M O

### *Objetivo*

*Verificar associação entre estado nutricional e fatores de riscos cardiovasculares tradicionais e não tradicionais em pacientes em hemodiálise.*

### *Métodos*

*Estudo transversal com 132 pacientes maiores de 18 anos em hemodiálise, analiando-se o estado nutricional por meio da avaliação subjetiva global. Informações sobre fatores de riscos tradicionais e não tradicionais para doenças cardiovasculares foram obtidos a partir de questionário estruturado e utilizou-se ainda o Escore de Framingham para avaliar risco cardiovascular. Na análise dos dados foram utilizados o teste Qui-quadrado ou teste Exato de Fischer, e Modelo de Regressão Log-binomial.*

### *Resultados*

*A desnutrição estava presente em 31,1% dos indivíduos. Tabagistas (p=0,016), ex-tabagistas (p=0,034) e pessoas com diabetes Mellitus (p=0,001), apresentavam maior percentual de desnutrição. Verificou-se que a desnutrição era 4,53 vezes mais prevalente em indivíduos diabéticos (95%CI: 1,99-10,27) e 2,26 vezes mais prevalente entre os ex-tabagistas (95%CI: 1,04-4,95). Indivíduos com desnutrição tinham 4,03 vezes mais prevalência do risco cardiovascular moderado a grave.*

### *Conclusão*

*Observou-se uma elevada prevalência da desnutrição e de outros fatores de riscos para doenças cardiovasculares. Dentre esses fatores, convém citar a diabetes Mellitus, o tabagismo e o ex-tabagismo que apresentaram associação com a desnutrição. Além disso, verificou-se que os indivíduos desnutridos tinham probabilidade maior de desenvolver doença cardiovascular em 10 anos.*

***Palavras-chave***: *Doenças cardiovasculares. Insuficiência renal crônica. Hemodiálise. Desnutrição.*

## I N T R O D U C T I O N

Prevalence of Chronic Kidney Disease (CKD) has been estimated to increase every year between 10 and 13% in the developed countries' adult population. In developing countries, CKD prevalence data are still limited and heterogeneous [1]. In Brazil, estimates indicate an increase in prevalence per year, with a dialysis treatment rate of approximately 610 patients per million, a growth of 3% per year, and estimated mortality rate of 19.9% of those patients [2].

Despite science advances, the mortality rate in this population is still considered high, and Cardiovascular Diseases (CVD) are the leading causes of death in patients with CKD, especially in patients on dialysis [3]. In this population, traditional cardiovascular risk factors (hypertension, diabetes *Mellitus*, hypercholesterolemia, hypertriglyceridemia) are accrued with nontraditional risk factors such as hyperhomocysteinemia, oxidative stress, altered calcium and phosphorus metabolism, anemia, inflammation and malnutrition [4].

In addition to being considered a cardiovascular risk factor, the nutritional status of patients is a predictor of clinical evolution during hemodialysis treatment [5]. The high prevalence of malnutrition is common for several reasons, such as decreased food intake, hormonal and gastrointestinal disorders, as well as loss of amino acids, peptides and vitamins during dialysis. One of the main factors associated with higher morbidity and mortality in hemodialysis patients is the protein energy malnutrition [6].

Based on the foregoing, it is possible that malnutrition associated with other cardiometabolic risk factors increasingly raises mortality rates of CKD patients. Thus, this study aimed at verifying the association between nutritional status and traditional and nontraditional cardiovascular risk factors in hemodialysis patients.

## METHODS

Cross-sectional study, conducted with 132 patients, in a nephrology clinic, *Clínica do Rim* in *Bahia*, Brazil, from October to December 2017.

Patients older than 18 years, who had been registered in the clinic's hemodialysis program for more than 90 days, and who were able to consent to their participation signing the Free and Informed Consent Form were enrolled in the study. Individuals who were physically or mentally disabled or who refused to answer in any stage of the study were excluded. The following patients were also not included in the study: those diagnosed with congestive heart failure (grades III and IV), systemic lupus erythematosus, cancer, acquired immunodeficiency syndrome, with previous peritoneal dialysis or who had undergone kidney transplantation.

Clinical information was collected from the patients' medical records such as diagnosis of hypertension and diabetes *Mellitus*, dry weight and height (for calculation of Body Mass Index [BMI]), and results of biochemical exams performed up to 30 days before the investigation. Sociodemographic information was obtained through a self-reporting questionnaire.

For the assessment of nutritional status, the Subjective Global Assessment (SGA) validated for CKD patients was used, sorting patients as well-nourished (score 6-7), with mild or moderate malnutrition (score 3-5) and severe malnutrition (score 1-2) [7]. For the association analysis, the variable was re-categorized as well-nourished and malnourished, including in the latter category any degree of malnutrition.

Traditional risk factors for CVD were: male gender, over 60 years of age, presence of hypertension, diabetes *Mellitus*, smoking, dyslipidemia and hypertriglyceridemia, which were categorized according to the recommendations of the *Sociedade Brasileira de Cardiologia* [8]. Serum Total Cholesterol (TC) and triglyceride levels were determined by automated enzymatic colorimetric method. The High Density Lipoprotein (HDLc) level was measured by direct method and the Low Densinty Lipoprotein (LDL) levels using the Friedewald Formula [9].

Non-traditional CVD risk factors assessed included: Parathyroid Hormone (PTH), serum calcium and phosphorus, calcium x phosphorus product, hemoglobin levels according to the values recommended by the Kidney Disease Outcomes Quality Initiative (K/DOQI) [10] and malnutrition. For the analysis of the intact parathyroid hormone the Chemiluminescence method was used and for the dosages of calcium and phosphorus, the Titrimetric method and the Basques and Lustosa method were used, respectively.

To assess Cardiovascular Risk, the Framingham Score was used. This method is able to estimate the risk of developing cardiovascular disease over the next ten years. Cardiovascular risk was estimated as being low (<6%), moderate (6-20%) and high (≥20%) [11]; this is a parameter used by the scientific community to assess cardiovascular risk.

Analyses were performed using the Statistical Package for Social Science (SPSS) 15.0. The Shapiro-Wilk test verified the normality of each variable distribution.

In the descriptive analysis continuous variables were presented as mean ± standard deviation (for parametric data) or median and interquartile range (for nonparametric data), and the categorical variables were shown as percentages. A descriptive analysis was performed according to nutritional status, and the association with traditional and nontraditional cardiovascular risk factors was evaluated, as well as the association of the nutritional status with the Cardiovascular Risk by applying the Chi-square test or Fisher's Exact Test. A log-binomial regression analysis was also performed with malnutrition and cardiovascular risk as the outcome. For comparative analysis, the sample was stratified into two groups according to nutritional status: well-nourished and malnourished. In the regression, cardiovascular risk was recategorized as low and moderate/high. In all statistical tests a significance level of 5% was adopted.

The protocol of this study was approved by the *Universidade Federal do Recôncavo da Bahia* Research Ethics Committee (No. 2.223.071).

## RESULTS

The CKD individuals evaluated in this study were 52.3 (±12.4) years old. Their mean hemodialysis time was 132.2 (±121) months.

It was found that 68.9% of the individuals were well nourished and 31.1% were malnourished. Out of these, 30.3% presented with mild to moderate malnutrition and 0.8%, with severe malnutrition.

Among the malnourished individuals, 63.4% were adults; 85.6% classified themselves as black or mulattos; 48.8% were illiterate and 82.9% had a minimum monthly income of 01 minimum wage. The characterization of those individuals according to their nutritional status is described in Table 1, with no statistically significant difference between the variables presented and nutritional status.

It was also observed that 22.7% of the individuals were thin according to their BMI, and that only 39% of the individuals classified as malnourished by the SGA were thin.

Regarding the traditional, demographic and behavioral risk factors, it was observed that, in general, 27.3% of the individuals studied were elderly and 62.1% male. Smoking frequency was

**Table 1**. Characterization of individuals with chronic kidney disease on hemodialysis according to nutritional status. *Salvador* (BA), 2018.

| Characteristics | Total | | Well nourished | | Malnourished | | p-value* |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| *Gender* | | | | | | | |
| Male | 82 | 62.1 | 55 | 60.4 | 27 | 32.9 | 0.553 |
| Female | 50 | 37.9 | 36 | 39.6 | 14 | 34.1 | |
| *Age* | | | | | | | |
| Adult | 96 | 72.7 | 70 | 76.9 | 26 | 63.4 | 0.107 |
| Elderly | 36 | 27.3 | 21 | 23.1 | 15 | 36.6 | |
| *Color (self report)* | | | | | | | |
| Caucasian | 17 | 12.9 | 15 | 16.5 | 2 | 4.9 | |
| Mulatto | 66 | 50.0 | 42 | 46.2 | 24 | 58.5 | 0.192 |
| Black | 47 | 35.6 | 32 | 35.2 | 15 | 36.6 | |
| Yellow | 2 | 1.5 | 2 | 2.1 | 0 | 0 | |
| *Education* | | | | | | | |
| Illiterate | 53 | 40.2 | 33 | 36.3 | 20 | 48.8 | |
| Elementary | 47 | 35.6 | 37 | 40.7 | 10 | 24.4 | 0.268 |
| Medium | 27 | 20.5 | 17 | 18.7 | 10 | 24.4 | |
| Higher | 5 | 3.7 | 4 | 4.3 | 1 | 2.4 | |
| *Income* | | | | | | | |
| Up to 1 MW | 116 | 87.9 | 82 | 90.1 | 34 | 82.9 | 0.182 |
| Between 1 and 3 MW | 14 | 10.6 | 7 | 7.7 | 7 | 17.1 | |
| Between 3 and 6 MW | 2 | 1.5 | 2 | 2.2 | 0 | 0.0 | |
| *BMI* | | | | | | | |
| Thinness | 30 | 22.7 | 14 | 15.4 | 16 | 39.0 | |
| Eutrophy | 67 | 50.8 | 49 | 53.8 | 18 | 43.9 | 0.023 |
| Overweight | 25 | 18.9 | 20 | 22.0 | 5 | 12.2 | |
| Obesity | 10 | 7.6 | 8 | 8.8 | 2 | 4.9 | |

Note: *Chi-square Test and Fisher's Exact Test; MW: Minimum Wage; BMI: Body Mass Index.

3.8%, and only one patient consumed more than 20 cigarettes/day. However, the frequency of former smokers was 43.2%. Physical inactivity was evidenced in 92.4% of the patients assessed. Statistical analysis showed a statistically significant association between nutritional status and diabetes *Mellitus*, smoking and former smoker condition (Table 2).

Among the clinical factors, there was a high frequency of systemic arterial hypertension (57.6%), diabetes (32.6%), TC elevation (18.9%), hypertriglyceridemia (47.7%), high Low Density Lipoprotein (LDLc) levels (3.8%) and low HDLc levels in 61.4% of the subjects studied (Table 2).

Regarding nontraditional risk factors, the patients exhibited a mean serum phosphorus level of 5.97±1.62mg/dL; calcium x phosphorus was 58.46±22.01mg/dL and the mean hemoglobin concentration was 11.47±1.75mg/dL. Serum calcium median was 9.5mg/dL (9.0-10.1mg/dL) and PTH 290.5pg/mL (131.3-626.1pg/mL). However, in the sample stratified analysis there was no association between nutritional status and non-traditional risk factors ($p>00.5$) (Table 3).

**Table 2**. Traditional cardiovascular risk factors according to nutritional status in hemodialysis patients. *Salvador* (BA), 2018.

| Subjects | Total | | Well nourished | | Malnourished | | PR (95%CI)** |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| *Male* | | | | | | | |
| Yes | 82 | 62.1 | 55 | 60.4 | 27 | 65.9 | - |
| No | 50 | 37.9 | 36 | 39.6 | 14 | 34.1 | 1.19 (0.54 – 2.66) |
| *Elderly* | | | | | | | |
| Yes | 36 | 27.3 | 21 | 23.1 | 15 | 36.6 | - |
| No | 96 | 72.7 | 70 | 76.9 | 26 | 63.4 | 1.65 (0.71 – 3.87) |
| *Smoking** | | | | | | | |
| Yes | 5 | 3.8 | 1 | 1.1 | 4 | 9.8 | - |
| No | 127 | 96.2 | 90 | 98.9 | 37 | 90.2 | 1.85 (0.96 – 3.68) |
| *Former smoker** | | | | | | | |
| Yes | 57 | 44.9 | 35 | 38.9 | 22 | 59.5 | - |
| No | 70 | 55.1 | 55 | 61.1 | 15 | 40.5 | 2.26 (1.04 – 4.95) |
| *Arterial hypertension* | | | | | | | |
| Yes | 76 | 57.6 | 48 | 52.7 | 28 | 68.3 | - |
| No | 56 | 42.4 | 43 | 47.3 | 13 | 31.7 | 1.86 (0.83 – 4.16) |
| *Diabetes Mellitus** | | | | | | | |
| Yes | 43 | 32.6 | 21 | 23.1 | 22 | 53.7 | - |
| No | 89 | 67.4 | 70 | 76.9 | 19 | 43.3 | 4.53 (1.99 – 10.27) |
| *Sedentary lifestyle* | | | | | | | |
| Yes | 122 | 92.4 | 82 | 90.1 | 40 | 97.6 | - |
| No | 10 | 7.6 | 9 | 9.9 | 1 | 2.4 | 4.05 (0.49 – 33.17) |
| *TC >200mg/dL* | | | | | | | |
| Yes | 25 | 18.9 | 17 | 18.7 | 8 | 19.5 | - |
| No | 107 | 81.1 | 74 | 81.3 | 33 | 80.5 | 0.86 (0.32 – 2.34) |
| *TG >150mg/dL* | | | | | | | |
| Yes | 63 | 47.7 | 42 | 46.2 | 21 | 51.2 | - |
| No | 69 | 52.3 | 49 | 53.8 | 20 | 48.8 | 0.86 (0.40 – 1.85) |
| *HDL <40mg/dL (♂)* | | | | | | | |
| *<50mg/dL (♀)* | | | | | | | |
| Yes | 81 | 61.4 | 57 | 62.6 | 24 | 58.5 | - |
| No | 51 | 38.6 | 34 | 37.4 | 17 | 41.5 | 0.81 (0.37 – 1.76) |
| *LDL >160mg/dL* | | | | | | | |
| Yes | 5 | 3.8 | 2 | 2.2 | 3 | 7.3 | - |
| No | 126 | 96.2 | 88 | 97.8 | 38 | 92.7 | 7.76 (0.78 – 77.25) |

Note: *Chi-square Test and Fisher's Exact Test, *p*-value <0.05; **Log-binomial regression.
PR: Prevalence *Ratio*; TC: Total Cholesterol; TG: Triglycerides; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein.

According to the Framingham Score, 51.4% of the individuals assessed exhibited a moderate cardiovascular risk and 14.4% had a high risk of developing cardiovascular disease in the next 10 years. When comparing nutritional status, the vast majority of malnourished individuals (85.3%) had moderate or high cardiovascular risk, with a significant statistical difference (Table 4). In relation to well-nourished individuals (42.8% exhibited low cardiovascular risk).

**Table 3**. Nontraditional cardiovascular risk factors according to nutritional status of hemodialysis subjects. *Salvador* (BA), 2018.

| Subjects | Total | | Well nourished | | Malnourished | | p-value* |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| *PTH (>300pg/dL)* | | | | | | | |
| Yes | 65 | 49.2 | 45 | 49.5 | 20 | 48.8 | 0.943 |
| No | 67 | 50.8 | 46 | 50.5 | 21 | 51.2 | |
| *Calcium (>9.5mg/dL)* | | | | | | | |
| Yes | 65 | 49.2 | 48 | 52.7 | 17 | 41.5 | 0.23 |
| No | 67 | 50.8 | 43 | 47.3 | 24 | 58.5 | |
| *Phosphorus (>5.5mg/dL)* | | | | | | | |
| Yes | 76 | 57.6 | 52 | 57.1 | 24 | 58.5 | 0.881 |
| No | 56 | 42.4 | 39 | 42.9 | 17 | 41.5 | |
| *CaxP (>55mg/dL)* | | | | | | | |
| Yes | 67 | 50.8 | 47 | 51.6 | 20 | 48.8 | 0.76 |
| No | 65 | 49.2 | 44 | 48.4 | 21 | 51.2 | |
| *Hb (<13mg/dL)* | | | | | | | |
| Yes | 112 | 84.8 | 79 | 86.8 | 33 | 80.5 | 0.348 |
| No | 20 | 15.2 | 12 | 13.2 | 8 | 19.5 | |

Note: *Chi-square Test; PTH: Parathyroid Hormone; CaxP: Calcium x Phosphorus; Hb: Hemoglobin.

**Table 4**. Cardiovascular risk according to Framingham score according to nutritional status. *Salvador* (BA), 2018.

| Risk | Total | | Well nourished | | Malnourished | | PR (95%CI)** |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| Low Cardiovascular Risk* | 45 | 34.2 | 39 | 42.8 | 6 | 14.7 | - |
| Moderate Cardiovascular Risk* | 68 | 51.4 | 36 | 39.6 | 32 | 78.0 | 4.03 (1.53 – 10.63) |
| High Cardiovascular Risk* | 19 | 14.4 | 16 | 17.6 | 3 | 7.3 | |

Note: *Chi-square Test and Fisher's Exact Test, p-value <0.01; **Log-binomial regression evaluated nutritional status as a predictor of cardiovascular risk (low vs. moderate and high); PR: Prevalence *Ratio*.

The univariate log-binomial regression model found that former smokers (Prevalence *Ratio* [PR]: 2.26; CI95%: 1.04-4.95) and with diabetes *Mellitus* (PR: 4.53; CI95%: 1.99-10.27) have a higher prevalence of malnutrition (Table 2). By using cardiovascular risk as an outcome, malnourished individuals showed a higher prevalence of moderate to severe cardiovascular risk, according to the Framingham Score (PR: 4.03; CI95%: 1.53-10.63) (Table 4).

## DISCUSSION

It is known that the nutritional status of patients needs to be continuously monitored due to the important association between protein energy malnutrition and increased morbidity and mortality in hemodialysis patients. Regarding malnutrition, a high prevalence was found in the population assessed, in line with other literature data that indicate percentages ranging from 18.6% to 96.2% [12,13].

In a cross-sectional study conducted in Northeastern Brazil, with 58 patients on hemodialysis, a prevalence of almost 40% of malnutrition was observed [14], higher than the rate found in the present study. However, a study also conducted in Brazil, in the Midwest region, with 344 individuals, identified a malnutrition rate of 22.4% [15]. Such prevalence differences occur due to several factors, namely environmental and dietary diversity of each locality; population representativeness of each study; dialysis treatment time duration; health attention received; and socioeconomic conditions of the individuals. Malnutrition in these individuals has a complex etiology, possibly as a result of the disease itself and associated treatment factors that may cause decreased food intake, increased protein catabolism, and nutrient losses during hemodialysis [16].

Malnutrition may increase mortality in hemodialysis patients by reducing immunity, increasing the risk of infections, lowering serum protein levels, causing edema and increasing systemic complications during treatment.

Among the individuals studied, several traditional cardiovascular risk factors were present, especially hypertension. Cross-sectional studies performed by Havinder *et al.* [17] and Zhang *et al.* [18], in Malaysia and China, found hypertension prevalence rates of 74% and 92.3%, respectively, higher than those found in this study. And in Northeast Brazil, a study with 73 patients found that 65.8% were hypertensive [19]. Hypertension in hemodialysis patients is difficult to control due to its pathophysiology and complexity and represents a significant risk factor for cardiovascular events in that population.

Diabetes *Mellitus* is also a very common traditional risk factor, being one of the causes of CKD and the second most common etiology among hemodialysis patients in Brazil. Cohort study conducted in Brazil with 3.082 individuals found  20% diabetes prevalence [20], while Havinder *et al.* [17] found 36% diabetes prevalence. In the present study, individuals with diabetes *Mellitus* exhibited a 4.53 times greater probability of malnutrition, a result that expresses the importance of evaluating and monitoring traditional risk factors.

When analyzing non-traditional risk factors, high levels of phosphorus and calcium-phosphorus product were found in relation to the recommendation of international guidelines, which is consistent with the data of studies from other countries [21,22]. Scientific studies indicate that both are linked to arterial calcification of hemodialysis patients, especially when the individual is malnourished, increasing the chances of developing CVD [18,23]. In this study, it was also observed that the great majority of the individuals assessed had decreased serum hemoglobin levels, but there was no significant difference on account of their nutritional status, just like the results obtained by Espahbodi *et al.* [13]. It is likely that the high prevalence of anemia in these individuals is associated to reduced kidney erythropoietin production, acute and chronic inflammatory conditions and limited access to erythropoietin during dialysis [24].

In this study, it was found that smoking or being a former smoker and the presence of diabetes *Mellitus* are more prevalent in malnourished individuals than in non-malnourished individuals. According to the World Health Organization, smoking contributes to malnutrition because individuals buy tobacco at the expense of food (25). In addition, it was found that the percentage of malnutrition was high among individuals with moderate cardiovascular risk, according to the assessment by the Framingham score, a finding much higher than that obtained in the study by Huang *et al.* [26].

By analyzing the nutritional status as a risk factor for cardiovascular disease in those patients, it was observed, through the regression model, that individuals with malnutrition had a higher prevalence of moderate and high cardiovascular risk. In Tehran, a study with 291 hemodialysis patients

also found a significant association between malnutrition and increased risk of cardiovascular disease [27]. Moreover, Leavey et al. [28] found a significant association between malnutrition and morbidity and mortality associated with cardiovascular disease in patients undergoing hemodialysis.

This relationship between malnutrition and increased prevalence of cardiovascular risk may be attributed to high serum levels of inflammatory substances (such as C-Reactive Protein), common in malnourished patients, which are strong predictors of cardiovascular disease mortality.

## CONCLUSION

It was observed that malnutrition represents a frequent cardiovascular risk factor in patients on hemodialysis. In addition, there was a significant association between malnutrition and diabetes *Mellitus*, smoking and former smoker condition, and that individuals who were former smokers and with diabetes *Mellitus* exhibited a higher prevalence of malnutrition. An association between malnutrition and cardiovascular risk according to the Framigham Score was also found, indicating that malnourished individuals undergoing hemodialysis have a higher prevalence of moderate to high cardiovascular risk.

Further studies are required to highlight the risk factors in this population, clarify potential etiologies and help with the health care provided to hemodialysis patients.

## CONTRIBUTORS

About the article, all authors contributed to the conception and design; IS ANDRADE and LPM OLIVEIRA, contributed with data analysis and interpretation, review and approval of the final version of the article.

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