Nutritional status and interdialytic weight gain of chronic hemodialysis patients

ABSTRACT

Introduction: The nutritional status (NS) of patients on hemodialysis (HD) is a major concern and challenge. Malnutrition is common in these patients and is related to poorer clinical outcomes. Objectives: To assess the association between the NS and the interdialytic weight gain (IDWG) of patients with chronic kidney disease (CKD) on HD. Methods: Cross-sectional study with 322 patients older than 18 years. The NS was assessed by body mass index (BMI), percentage body fat estimated by the sum of four skinfolds (triceps, biceps, subscapular and supra iliac), lean body mass (LBM), serum creatinine and albumin and rate of nitrogen appearance (PNA). The IDWG was evaluated from the sum of the weight difference of 12 hemodialysis sessions (IDWGm). Results: Considering the sample into quartiles IDWGm, it was found that BMI, LBM, serum creatinine ($p < 0.001$) and PNA ($p = 0.011$) were directly correlated. There was no association between IDWGm and serum albumin. Using multivariate analysis, it was found that the prevalence of patients with BMI suitability and serum creatinine were significantly higher for patients in the bottom quartile with respect to the first IDWGm. Conclusion: The NS is positively associated with IDWG. The results point to the need for individualized assessment of IDWG and cautious in order not to generalize a recommendation that does not meet the expectations of maintaining and promoting the nutritional status of these patients.

Keywords: malnutrition; nutritional status; renal dialysis.

INTRODUCTION

The nutritional status of patients with chronic kidney disease (CKD) on hemodialysis (HD) is cause for concern and challenge for the multidisciplinary teams who assist them. Malnutrition is common in these patients and it is related to a worse prognosis.\textsuperscript{1-3} In addition to lower survival, malnourished patients on dialysis have higher morbidity,\textsuperscript{4,5} more functional disability\textsuperscript{6,7} and worst quality of life;\textsuperscript{2,4} hence the importance of monitoring and enhancing their nutritional status.

In this context, many are the studies\textsuperscript{8-12} indicating positive correlations between interdialytic weight gain (IDWG) and diet, which makes this parameter a putative indicator of the nutritional status of patients on hemodialysis.

Nevertheless, IDWG is also seen with clinically negative connotation, such as a risk for hypertension, congestive heart failure, hyponatremia, and complications related to the rapid removal of fluids during HD (hypotension, angina, arrhythmia and cramps).\textsuperscript{12-14} Thus, HD patients are often advised to limit their IDWG. However, such practice may result in adverse clinical outcomes, since the attempt to avoid fluid overload can jeopardize the nutritional statuses of these patients.\textsuperscript{9,12,15}
Pinpointing the IDWG range of patients with better nutritional status can help reduce the risk of malnutrition and bring about an ideal nutritional status. Thus, this study aimed to analyze the association between nutritional status and IDWG of CKD patients on Hemodialysis.

METHODS

This is a cross-sectional study carried out between May 2009 and March 2010, with clinically stable patients on regular HD programs from ten clinical centers in Goiânia, Goiás. The research project was assessed and approved by the Ethics in Human and Animal Research Committee from the University Hospital of the Federal University of Goiás (HC/UFG).

The study included patients over 18 years old, of both genders, on HD for over a year, anuric or with residual urine output < 100 ml/day and no clinical evidence of inflammatory and infectious processes in the past three months. The exclusion criteria were: use of central venous catheter, neoplasms, uncontrolled diabetes mellitus, chronic inflammatory diseases, severe lung disease and symptomatic heart failure (classes III and IV). Sample size was calculated considering the total number of individuals on HD in Goiania in 2008 (n = 1400), according to Municipal Health Secretariat data. For this estimate, we also considered the prevalence of malnutrition in this population as being 50%, with 95% confidence and 5% error. The required sample had 302 patients and at the end of the study, we evaluated 361 individuals in proportion to the total number of patients from each HD center. From all the patients evaluated, 322 were included in the final sample because they fit into all established selection criteria.

All patients underwent HD through an arteriovenous fistula every three weeks, with session time between 3.5 and 4 hours, dialysis with bicarbonate buffer solution, containing glucose and sodium concentration between 135 and 142 mEq/L. Among all patients, 91% used high performance polysulphone dialyzers, with an area between 1.2 and 2.2 m², while 9% used cellulose acetate dialyzers, with an area between 1.6 and 2.1 m².

Clinical data such as time in HD, pre-dialysis systolic blood pressure (SBP) and diastolic blood pressure (DBP), causes of CKD, comorbidities, dry weight and IDWG were learned from medical records of each patient and confirmed with the local medical staff. The mean arterial pressure was obtained by averaging 12 blood pressure measurements before the HD session. Hypertensive patients were those with mean BP ≥ 140/90 mmHg or those on anti-hypertensive medication. Mean IDWG (IDWGm) was calculated from the sum of the difference between the patient’s weight upon entering and leaving 12 HD sessions, and the IDWGm = Σ entry weight - Output weight ÷ number of sessions. The relative IDWG (IDWGr) was obtained by dividing the IDWGm by the patient’s dry weight, IDWGr = IDWGm ÷ dry weight X 100. An IDWGm ≤ 2.5 kg and an IDWGr ≤ 4.5% over the dry weight were considered normal values.

The demographic data we analyzed included gender and age. We assessed the nutritional status based on anthropometric and laboratory parameters, and we calculated the nitrogen appearance rate (NAR). The dialysis efficiency was estimated by calculating the Kt/V, using the value ≥ 1.2 as the cutoff point for normality - following current guidelines for HD adequacy.

Two nutritionists collected the anthropometric variables after the weekly intermediate dialysis session and they included height; triceps (TSF), biceps (DCB), subscapularis (DCSE) and suprailiac (DCSI) skinfolds, and soon after we calculated body fat percentage (% BF) and lean body mass (LBM). To ensure the adequacy, accuracy and precision of anthropometric measurements, we standardized the procedures carried out by the examiners, calculating the intra and inter observerTechnical Error (TEM), and comparing it with the measurement taken by a “gold standard” anthropometrist as proposed by Habicht.
Body mass index (BMI) was obtained from the ratio between the average dry weight and the square of height; and the patients’ nutritional statuses were classified as recommended by the World Health Organization (WHO). The skinfolds were measured in millimeters, using the Lange Skinfold Caliper according to the Lohman, Roche and Martorell protocol. Body fat (BF) was estimated as a percentage and in kg, from the sum of the four skinfold measurements, using the equations from Durnin & Womersley and Siri. LBM was calculated in kilograms by the difference between the dry weight and body fat.

The laboratory parameters analyzed were serum levels of albumin, creatinine and urea before and after HD. The biochemical measurements were performed on the Konelab 30 biochemical analyzer, and albumin was evaluated by the colorimetric method (bromocresol green); and serum creatinine and urea by the kinetic method. All analyses were performed by the University Hospital Clinical Laboratory - UFG. To interpret the nutritional status, we considered the following as normal values: serum creatinine ≥ 10 mg/dL, serum albumin > 4.0 g/dL; NAR ≥ 1.0 g/Kg and BMI > 23Kg/m².

Protein intake was estimated by calculating the protein equivalent of the nitrogen appearance rate (NAR)

\[(NAR) = \text{NAR (g/day)} = \frac{\text{pre-dialysis serum ureic nitrogen}}{[36.3 + (5.48) \times (Kt/V)] + 0.168}\]

**Statistical analysis**

Data was double entered and subsequently validated. After validation and consistency analysis, the data was analyzed using the Statistical Package for Social Sciences, version 18.0 for Windows (SPSS, Inc. Chicago) and presented as mean, standard deviation and frequency. All continuous variables were previously evaluated for normality using the Kolmogorov-Smirnov test, considering a \(p \geq 0.05\) as normal.

The bivariate analysis among the IDWGm quartiles and demographic, clinical and nutritional characteristics were performed by the Pearson chi-square test for categorical variables and ANOVA, and Kruskal Wallis test for continuous variables. Mean differences between groups were analyzed by the Tukey test.

Associations between among IDWGm quartiles with indicators of nutritional status: serum creatinine ≥ 10 mg/dL and BMI ≥ 23 kg/m² were analyzed by the Poisson regression model with robust variance adjusted for clinical and demographic conditions. We included in the regression the variables in the bivariate analysis that had significance below 20% \((p < 0.20)\). The level of significance was set at \(p < 0.05\).

**Results**

Table 1 depicts the general characteristics of the patients. We had 322 patients analyzed, aged 19-90 years, 76% adults and 24% older than 60 years. The HD treatment time ranged from 13 to 303 months. The IDWGm was above the recommended, the IDWGr was within the expected range, although it is important to point out that 41.6% of patients had IDWGr > 4.5%. Hypertensive nephrosclerosis was the most frequent cause of CKD (39.4%), followed by chronic glomerulonephritis (20.2%) and diabetes (14.6%), while the most prevalent comorbidity was hypertension (68%).

The population showed, on average, adequate levels for BMI, with 54% having optimal values for HD patients (BMI > 23 kg/m²). The prevalence of underweight patients (BMI < 18.5 kg/m²) was 8%, while normal weight (BMI between 18.5-24.9 kg/m²) and overweight (BMI ≥ 25 kg/m²) patients totaled 60% and 32%, respectively.

As for laboratory data, our sample had a suitable average level for albumin, with 64% of patients presenting values above 4.0 g/dL. However, serum creatinine was, on average, below recommended values, with 56% of patients with values below the ideal for HD patients. On average, NAR levels were as recommended, although the percentage of patients with lower levels was 53%.
Table 2 depicts the clinical and demographic characteristics according to IDWGm distribution by quartiles. The prevalence of hypertension was 68%. Average blood pressure levels were not associated with IDWGm. Age and gender were associated with IDWGm; the number of elderly patients was significantly lower in the last quartile in relation to the other quartiles ($p < 0.001$); and females were associated with lower IDWG ($p < 0.001$).

There was strong association between IDWGm and nutritional parameters (Table 2). Patients in the highest IDWGm quartile had higher body weight, BMI and LBM ($p < 0.001$), higher levels of serum creatinine ($p < 0.001$) and higher NAR ($p = 0.011$) compared to those in the other quartiles. IDWGm was not associated with serum albumin levels. Considering the BMI for nutritional diagnosis of the population, there was a significantly higher number of patients with low body weight (supposedly malnourished) in the first two quartiles of IDWG. The number of well-nourished patients was statistically higher in the last two quartiles, while those who were overweight (supposedly better fed) were associated with the higher range of interdialytic weight gain. Patients with better nutritional status, according to the investigated parameters, had average IDWGm of $4.1 \pm 0.6$ kg and IDWGr of $5.9 \pm 1.3\%$.

After a multivariate analysis, we concluded at the prevalence of patients with adequate BMI ($> 23$ kg/m$^2$) in the last quartile of IDWGm was 79% higher (PR = 1.79; 95% CI: 1.33 to 2.4) compared to the first quartile, while the prevalence of adaptation to serum creatinine was 52% higher (PR = 1.52; 95% CI: 1.01 to 2.3) (Table 3).

Discussion

Although most patients in this study had BMI and serum albumin levels as expected, the assessment of other parameters such as serum creatinine and NAR indicated impaired LBM and/or impaired protein ingestion. These findings suggest a common problem to the population in HD: poor or inadequate dietary intake associated with the most common cause of impairment to the nutritional status. Nonetheless, one of the limitations of this study was not evaluating the direct contribution of food consumption on the IDWG.

Until recently, the ideal and excessive IDWG were arbitrarily interpreted. Currently, it is recommended that patients on HD should not exceed 2.0 to 2.5 kg in absolute terms, or
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4 to 4.5% of IDWG on the dry weight during the interdialytic period. However, a higher IDWG may be justified for patients with higher body weight, especially when associated with increased LBM, as demonstrated in this study. Different studies also support the hypothesis of better nutritional status in patients with IDWGr > 4.5%, suggesting that the current cutoff point proposed for the IDWG may not be realistic regarding optimal nutritional status.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Clinical, Demographic and Nutritional Characteristics According to the Mean Interdialytic Weight Gain Quartiles of Patients in Hemodialysis - GO, 2010 (n = 322)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDWGr (%)</td>
<td>1.7 ± 0.3a</td>
</tr>
<tr>
<td>Time in HD (months)</td>
<td>55.2 ± 42.9</td>
</tr>
</tbody>
</table>

a,b,c,d Mean values of the same line with equal letters are statistically significant among each other (p ≤ 0.05). HD: hemodialysis; Kt/V: dialysis adequacy index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; BF: body fat; LBM: lean body mass; NAR: ureic nitrogen appearance rate; * ANOVA; **χ² test; *** Kruskal Wallis.
for patients on HD, especially considering the nutritional indicators and their respective cut-off points used in this study. Importantly, an ideal nutritional indicator should be able to predict clinical outcomes and identify patients who need nutritional intervention.31

In this study, female patients and the elderly had lower IDWG, while individuals with higher BMI and LBM, and higher levels of serum creatinine and NAR had higher IDWG. These results confirm data already published in the literature, i.e. IDWG diminishes with advancing age. Of the 77 elderly enrolled in the study, more than 90% were allocated to the first three IDWG quartiles. Yang et al.21 previously demonstrated lower IDWG in patients aged over 65 years. Other studies have also found a negative correlation between age and IDWG.11,36

Young patients, more metabolically active, tend to have higher food and water intake, determining factors for the IDWG.10,37,38 These findings corroborate the fact that younger patients on HD are subject to greater IDWG because of their metabolic response. It would also signal that the elderly on HD, emerging population under this condition, need to be on stricter nutritional monitoring, because a lower IDWG may also be indicative of poor dietary intake, making this group more susceptible to malnutrition and all its consequences.

The lower IDWG found for females is due in part to the fact the IDWG be proportional to body weight,36 and there was a lower total body mass for women compared to men in this study (results not shown).

Consistent with previous studies,11,39 we found a positive association between BMI and IDWG. BMI is considered an important marker of nutritional status for patients on HD. Unlike the general population, studies involving HD patients suggest that overweight is associated with better clinical outcome,39-44 with BMI above 23 kg/m² listed as lower risk for morbimortality.16,40,41 Evidence indicates, however, this condition is limited to those with normal or elevated LBM,45 a condition seen among the patients in the bottom IDWG quartile in this study.

The largest number of patients with adequate BMI was represented by the last IDWG quartile. This group is also highlighted by presenting significantly higher LBM than the other, suggesting higher energy spending and consumption. Consequently, the higher proportion of metabolically active tissue could explain the higher IDWG so as to justify the higher NAR and serum creatinine levels.

Several studies8,35,39 point out positive association between serum creatinine and IDWG, considering this marker also as an independent predictor of IDWG39 and suggesting that patients with higher LBM and/or protein intake, a favorable prognostic condition for this population29,45,46 may have higher IDWG. Although serum creatinine levels indicative of malnutrition in HD patients are not known, its prognostic capacity is evidenced in several studies,47-49 with survival directly proportional to their serum level. Mortality increases when serum creatinine levels are below 10 mg/dL.31,47-49

In this study, the last IDWGm quartile had patients with more adequate levels of serum

**Prevalence Ratio (PR) * for Interdialytic Weight Gain for Patients in Hemodialysis. Goiânia, GO - 2010, (n = 322)**

<table>
<thead>
<tr>
<th>Variables</th>
<th><strong>BMI &gt; 23kg/m²</strong></th>
<th>p</th>
<th>*<strong>Serum creatinine ≥ 10mg</strong></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDWGm ≤ 2.10 kg</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDWGm 2.11-2.70 kg</td>
<td>1.27 (0.93 - 1.73)</td>
<td>0.121</td>
<td>1.15 (0.75 - 1.75)</td>
<td>0.509</td>
</tr>
<tr>
<td>IDWGm 2.71-3.40 kg</td>
<td>1.52 (1.14 - 2.03)</td>
<td>0.004</td>
<td>1.39 (0.94 - 2.10)</td>
<td>0.509</td>
</tr>
<tr>
<td>IDWGm &gt; 3.40 kg</td>
<td>1.79 (1.33 - 2.40)</td>
<td>&lt; 0.001</td>
<td>1.52 (1.01 - 2.30)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

* Poisson regression - 95%CI; ** Model adjusted for gender, age, creatinine, NAR and time in HD; *** Model adjusted for gender, age, BMI, NAR and time in HD.
creatinine, which may represent a greater advantage in terms of survival for patients with higher IDWG. This hypothesis, however, remains controversial, since some studies have reported longer survival,\(^{11,39}\) while a more recent study involving over 34,000 patients reported that, after adjusted analysis, regardless of nutritional status, those with higher IDWG had higher rates of cardiovascular mortality and mortality by other causes.\(^{8}\) Indeed, these results reinforce the importance of investigating strategies that mitigate or reduce the exposure time to water retention without jeopardizing the nutritional status of this population.

About 60-90% of hemodialysis patients had hypertension,\(^{20}\) a result similar to that found in this study, and different from the one reported by Lopez-Gomez \emph{et al.}\(^{11}\) IDWG was not associated with hypertension. Testa & Plou\(^{10}\) found results similar to those observed in this study. One cannot ignore that BP control mechanisms used for dialysis patients are multifactorial and complex.

In this study, there was no difference between serum albumin according to IDWG. Although serum albumin stands out as a strong clinical prognostic factor for the dialysis population,\(^{49,50}\) its use as a marker of nutritional status is questionable, since serum levels may reflect not only the protein consumption, but different clinical situations, such as inflammation\(^{51}\) and superhydration.\(^{52}\) Thus, in this study it is likely that serum albumin behaved much more like a clinical indicator, highlighting those patients with fewer serious comorbidities and less inflammatory activity than necessarily well-nourished patients.

Regarding NAR, although there is no consensus that more IDWG can confer benefits to the population in HD, the results observed in this study confirm the hypothesis that protein intake is one of the determinants of this variable. Although a causal association between protein intake and nutritional status of dialysis patients is not well defined,\(^{46}\) different studies indicate that low intake of this nutrient is associated with worse outcomes.\(^{6,46,53}\) Thus, clinically stable HD patients need to reach a NAR of at least 1.0 g/kg of weight.\(^{22}\)

The results obtained in this study suggest that the IDWG may reflect the balance between nutritional demand and maintenance of body reserves. Regardless of gender, age and clinical conditions, patients in this study with higher BMI, LBM and/or higher protein intake, as evidenced by serum creatinine levels, had higher IDWG.

Similar to this study, Hecking \emph{et al.}\(^{36}\) also found better performance of nutritional indicators (PCR/NAR and serum creatinine) among patients from countries which IDWGr frequency, they termed as excessive (> 5.7%), was higher. Certainly, a higher IDWG can serve as a positive marker of food intake, for the satisfaction of energy and protein demands may be associated with increased fluid intake, leading to a higher IDWG.\(^{9,10,12,36}\)

In this context, IDWG interpretation according to suitability for nutritional indicators may be an alternative. To discriminate against a high IDWG resulting from high intake hydrosaline or related to successful dietary intake is mandatory for clinical monitoring of these patients. Both the registration or food recall can be instruments for evaluating such events because they enable the identification both of the habit as well as inadequate food intake, enabling relevant interventions.

HD patients should be continuously advised to limit the intake of salt and foods high in sodium, in order to enhance thirst control, favoring the lower fluid intake and IDWG, and not inadvertently directed to control food intake in order to limit water retention.

As this is a cross-sectional study, it is not possible to demonstrate a causal relationship among the variables investigated. However, this study conducted with a representative sample of patients from one of the capitals of the central region of Brazil has enabled the evaluation of the nutritional status of this population and its association with a conflicting variable and one of important clinical
interest, so that the actual outcomes can guide strategies for clinical management and intervention.

CONCLUSION

Nutritional status was positively associated with the IDWG of the population evaluated in this study. The results point to the need for individualized and careful evaluation of the IDWG in order to not generalize one IDWG recommendation that does not meet the expectations of ideal nutritional status maintenance and promotion for these patients.

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