


Malnutrition associated with inflammation in the chronic renal patient on hemodialysis

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SUMMARY

INTRODUCTION: *Malnutrition-Inflammation-Atherosclerosis Syndrome is very frequent in patients with chronic kidney disease on haemodialysis. In these patients, the inflammation associated with malnutrition is observed by the Malnutrition-Inflammation Score.*

OBJECTIVE: *To analyse the relationship between malnutrition-inflammation-atherosclerosis syndrome and anthropometric and biochemical parameters of patients on haemodialysis.*

METHODS: *A cross-sectional study was performed at the Haemodialysis Clinic of the Barão de Lucena Hospital, Recife, Brazil, between July and August 2016, with patients cared at the clinic for at least six months. Patients with amputees, hospitalized, visually impaired, HIV positive, with catheters in the neck, ascites and/or oedema, and those who were unable to provide information at the time of the interview were excluded. The patients were submitted to anthropometric evaluation for the classification of the nutritional status by waist circumference, neck circumference, body mass index, waist-to-hip ratio and waist-to-height ratio. Nutritional status related to inflammation was measured by the Malnutrition-Inflammation Score and nutritional status assessment using biochemical indicators that used urea, creatinine and albumin.*

RESULTS: *Twenty-seven individuals of both genders, adults and elderly, aged 51.3 ± 13.3 years old participated in the study. The anthropometric evaluation showed that most of the population presented cardiovascular risk. The biochemical evaluation reported low frequencies of malnutrition. Malnutrition-Inflammation-Atherosclerosis syndrome was evidenced in 3.7% of the patients. The Malnutrition-Inflammation Score had a moderate negative correlation with body mass index, waist circumference, neck circumference, waist-to-height ratio and creatinine.*

CONCLUSION: *The correlation seen among the parameters suggests that most of the parameters evaluated can be used as an indirect indicator of malnutrition-inflammation-atherosclerosis syndrome.*

KEYWORDS: *Renal insufficiency, chronic. Renal dialysis. Malnutrition. Inflammation.*

INTRODUCTION

The change in the diet pattern of the Brazilian population contributes greatly to the high prevalence of chronic noncommunicable diseases (NCDs), such as systemic arterial hypertension (SAH), dyslipidaemias, obesity and diabetes mellitus (DM)¹. These

pathologies, in turn, tend to injure several organs, such as the kidneys. The nephropathies group encompasses several diseases that affect the kidneys and that can subsequently lead to chronic kidney disease (CKD), characterized by irreversible, slow

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and progressive loss of renal function, being a major public health problem², mainly due to its social and economic implications³.

Among the types of treatments available for CKD, haemodialysis (HD) is one of the most used. This method filters and purifies undesirable substances from the blood, such as urea and creatinine⁴, and is considered a good tool for the treatment of CKD and for the clinical improvement of the patient. Despite its benefits, HD can cause some undesirable changes to the dialytic patient, such as hypotension, cramps, protein loss and inflammatory process⁵.

Malnutrition-Inflammation-Atherosclerosis (MIA) occurs in chronic kidney patients on HD due to several factors. Anorexia, presence of obesity, metabolic disorders and the dialysis itself are among the main causes of this syndrome, leading to the loss of body proteins and to the production and action of pro-inflammatory cytokines⁶.

In patients with CKD on HD, it is possible to observe the presence of inflammation associated with malnutrition by means of the Malnutrition-Inflammation score (MIS)⁷. This method can replace parameter values that quantify the inflammatory process, such as interleukin-6 (IL-6) and ultra-sensitive C-reactive protein⁸.

Thus, this study aimed to evaluate the possible correlation between MIS and nutritional parameters of chronic renal patients on HD, and it was also intended to identify, among the indicators studied, those that could be used as a marker of MIA syndrome with low cost, easy application and reduced time.

METHODS

A cross-sectional study that was carried out at the Haemodialysis Clinic of the Barão de Lucena Hospital (HBL), Recife, Brazil, between July and August 2016. The study participants were patients with CKD of both genders, adults and elderly, attended at the clinic for at least six months. Patients with amputees, hospitalized, HIV positive, with catheters in the neck, ascites and/or oedema, and those who, for some reason, were unable to provide information at the time of the interview and anthropometric evaluation were excluded.

The characterization of the sample was made based on socio-demographic (gender, age, socioeconomic conditions), clinical (comorbidities) and lifestyle (smoking, alcoholism and physical activi-

ty practice) parameters. Socioeconomic conditions were assessed based on the criteria of the Brazilian Association of Population Studies (Abep)⁹, while the demographic and clinical data were collected from the patient's chart. The practice and type of physical activity were analysed according to parameters of the Brazilian Society of Cardiology; Brazilian Society of Hypertension; Brazilian Society of Nephrology¹⁰. Alcohol consumption was classified as "consumes" and "does not consume", and the smoking aspect according to Silva et al.¹¹, which rates the individual as a smoker, former smoker and never smoked.

The patients were submitted to anthropometric evaluation to rate their nutritional status. The measures were carried out by the head of the research, previously trained, in order to minimize errors in measurements. The following measures were taken: weight, height, waist circumference (WC), hip circumference (HC), neck circumference (NC), body mass index (BMI), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR).

Dry weight was obtained on a Welmy scale, with a capacity of 200 kg (440 pounds). Height was measured by an aluminium stadiometer coupled to the scale. Wheelchair and elderly patients had their height estimated by the formula proposed by Chumlea et al.¹². Both weight and height were determined according to the technique standardized by Lohman et al.¹³.

WC and HC measurements were performed using an inelastic tape, according to a technique described by Lohman et al.¹³. The cut-off points for WC and WHR rating were based on Cook et al.¹⁴ and Pereira¹⁵, respectively. For the WHtR indicator, the calculation proposed by Haun et al.¹⁶ was considered and the cut-off points used were those of Pitanga and Lessa¹⁷. The NC measurement was made and rated according to Bem-Noun et al.¹⁸. All anthropometric measurements were performed twice, after the dialysis session, considering the mean values.

The nutritional status of the patients related to inflammation was measured by the MIS, comprised of ten components, seven of them being from the Global Subjective Assessment and three items (BMI, serum albumin and total iron-binding capacity - TIBC)⁷. Each component of the MIS has four levels of severity, being scaled from 0 (normal) to 3 (very severe). The final score ranges from 0 to 30.

The assessment of nutritional status according to the biochemical indicators used urea, creatinine and albumin. The cut-off for normality of these parame-

ters was according to Riella and Martins¹⁹, with urea equal to 130-200 mg/dL, creatinine at 7-12 mg/dL and albumin at 3.5-5 g/dL. All values were collected from the patient's chart.

Statistical analysis was performed with the help of the Statistical Package for Social Sciences - SPSS version 13.0 (SPSS Inc., Chicago, IL). Continuous variables were tested for normality of distribution by the Kolmogorov Smirnov test (to evaluate the symmetry of the variables distribution curve). Data from the normal distribution variables were expressed as mean and standard deviation. Categorical data were expressed in frequency. To verify the correlation between MIS and the anthropometric and biochemical variables, the Pearson correlation test was used, values between 0.3 and 0.5, whether positive or negative, were considered as weak correlation, whereas values between 0.5 and 0.7, as a moderate correlation. Factors for which the p-value was less than 0.05 were considered to be significantly associated.

The study was approved by the Human Research Ethics Committee of the Hospital Otávio de Freitas, on May 3, 2016 (CAAE: 54883816.8.0000.5200), based on ethical standards for research involving human beings, contained in resolution 466/2012 of the National Health Council. Participants were previously informed of the objectives of the research, as well as the methods to be adopted. All patients who agreed to participate and were within the eligibility criteria of the research signed the Informed Consent Term.

RESULTS

Twenty-seven individuals of both genders, aged 51.3 ± 13.3 years old and haemodialysis time of 2.59 ± 1.78 years, participated in the study. Table 1 shows the sociodemographic, clinical and lifestyle characteristics presented by the participants of the study, in which the similarity in the frequency between the genders, prevalence of sedentary life and SAH, followed by DM, is observed in the sample studied.

Table 2 shows the frequency of nutritional indicators. Regarding the anthropometric parameters, the majority of the evaluated population was at cardiovascular risk, according to the measures of circumferences used. According to the biochemical parameters, low frequencies of risk of malnutrition stand out; the MIS score assessment identified 3.7% of patients with MIA, with a mean score of 4.89 ± 2.32 .

The correlation between MIS and anthropometric

and biochemical parameters can be seen in Table 3, which highlights the moderate negative correlation between MIS and serum creatinine ($r = -0.644$, $p = 0.000$). It is noted that MIS presented a moderate negative correlation with BMI, NC, WC and serum creatinine.

DISCUSSION

The majority of the study population were adults and males. Other studies have shown a higher prevalence of males compared to females in haemodialysis clinics²⁰, while age has been described predominantly higher (59.4 ± 9.9 years old), according to data from the Brazilian Society of Nephrology²¹.

Regarding the cause of CKD, studies report that SAH, followed by DM, are the main etiological factors of CKD²², and this is quite concerning, since these pathologies are related to higher mortality²³. Databases

TABLE 1 – SOCIO-DEMOGRAPHIC, CLINICAL, AND LIFESTYLE CHARACTERISTICS OF CHRONIC RENAL PATIENTS FROM HAEMODIALYSIS CLINICS OF HOSPITAL BARÃO DE LUCENA, RECIFE – PE / 2016.

Variables	Quantity (%)
Men	15 (55.6)
Women	12 (44.4)
Level of Education	
Illiterate / Uncomplete Primary School	7 (25.9)
Complete Primary School	6 (22.2)
Complete Secondary School	2 (7.4)
Further Education	12 (44.4)
Economic Classification	
B1	2 (7.4)
B2	3 (11.1)
C1	7 (25.9)
C2	10 (37)
D	5 (18.5)
Physical Activity	
Yes	3 (11.1)
No	24 (88.9)
Ingestion of Alcoholic Beverages	
Yes	2 (7.4)
No	25 (92.6)
Smoker	
Never Smoker	20 (74.1)
Former Smoker	7 (25.9)
Comorbidities	
Hypertension	24 (88.8)
Diabetes	8 (29.6)
Dyslipidaemia	1 (3.75)
Others	2 (7.4)

TABLE 2. FREQUENCY OF NUTRITIONAL INDICATORS IN CHRONIC RENAL PATIENTS FROM HAEMODIALYSIS CLINICS OF HOSPITAL BARÃO DE LUCENA, RECIFE – PE / 2016.

Variables	Quantity (%)
Waist Circumference	
With Cardiovascular Risk	18 (66.7)
Without Cardiovascular Risk	9 (33.3)
Neck Perimeter	
With Cardiovascular Risk	21 (77.8)
Without Cardiovascular Risk	6 (22.2)
Waist-to-Hip Relation	
With Cardiovascular Risk	16 (64)
Without Cardiovascular Risk	9 (36)
Waist-to-Height Relation	
With Cardiovascular Risk	18 (66.7)
Without Cardiovascular Risk	9 (33.3)
Albumin	
Normal	25 (92.6)
Decreased	2 (7.4)
Creatinine	
Normal	21 (80.8)
Decreased	5 (19.2)
Urea	
Normal	21 (77.8)
Decreased	6 (22.2)
MIS	
Eutrophics / Light Undernourished	26 (96.3)
Moderate Undernutrition	1 (3.7)

MIS: Undernutrition – Inflammation Score

TABLE 3 – CORRELATION OF UNDERNUTRITION – INFLAMMATION SCORE (MIS) WITH ANTHROPOMETRIC AND BIOCHEMICAL PARAMETERS OF CHRONIC RENAL PATIENTS FROM HAEMODIALYSIS CLINICS OF HOSPITAL BARÃO DE LUCENA, RECIFE / 2016.

Parameters	Correlation Ratio ^a	p-value
IMC	-0.599	0.001**
Waist Circumference	-0.509	0.007**
Neck Perimeter	-0.541	0.004**
Waist-to-Hip Relation	-0.315	0.125
Waist-to-Height Relation	-0.466	0.014*
Serial Creatinine	-0.644	0.000*
Serial Urea	0.284	0.152
Serial Albumin	-0.189	0.345

IMC: Body Mass Index; ^aPearson Correlation; *p<0.05; **p<0.01

from the USRDS in 2009 showed that, generally, of diabetic patients initiating the haemodialysis process, only 30% survive after five years of treatment²⁴.

Most of the patients who participated in the study did not perform any kind of physical activity, and this

reality is quite common among patients who are on HD. In other studies with CKD on HD performed in Brazil, there is also a high prevalence of sedentary patients, with a predominance of up to 73.1% of sedentary lifestyle²³. Dyspnoea, anaemia, fatigue, generalized muscle weakness, SAH and other factors that constitute uremic syndrome are the main causes of low adherence of CKD patients on HD to physical exercise²⁵.

In the present study, WC showed a higher cardiovascular risk than a survey carried out in 2013 in the Northeast region of Brazil, in which the WC reported was increased in 51.4% of the sample, and this prevalence was higher in females²⁶. WC is considered a good predictor of abdominal fat and cardiovascular risk²⁷. In addition, abdominal obesity, evaluated by WC, seems to be closely related to age and genetic factors, eating behaviour and reduction in the level of physical activity²⁸.

The highest percentage of inadequacy was observed by the NC, which also assesses the risk for cardiovascular diseases. The neck region is responsible for a high release of systemic fatty acids. For this reason, the cardiovascular risk of NC is compared to the cardiovascular risk evidenced by WC²⁹. In addition, NC is shown to be connected to insulin resistance indicators, such as fasting glycaemia and glycated haemoglobin, in addition to the PCR and BMI³⁰.

The WHtR measure also assesses the presence of cardiovascular risk. Increased WHtR is slightly related to increased risks of cardiovascular events over a period of up to ten years²⁷.

The high risk of cardiovascular disease seen in this study by the anthropometric parameters can be justified by several factors. Chronic kidney disease is considered to be an independent factor for cardiovascular events alone and the drop in glomerular filtration rate (GFR) is directly proportional to the risk of CVD³¹. Some research has shown that elevation of pro-inflammatory cytokines and the haemodialysis process itself, due to characteristics such as duration and time interval between dialysis sessions, are also major cardiovascular risk factors, since they cause cardiac stress³². In addition to these possible causes, other factors such as hyperphosphatemia, dyslipidaemia, sedentary lifestyle, high calcium-phosphorus product, SAH and DM are related to cardiovascular risk in dialysis patients³³.

Among the anthropometric parameters studied, the WHR was the only one that did not present a correlation with MIS, suggesting that this indicator

would not be adequate to evaluate the risk of MIA syndrome. In fact, in the literature there are several limitations to the use of WHR to assess nutritional diagnosis, such as failure to detect the proportional increase of the waist and hip, the influence of hormonal modification and imprecision of internal fat disposition.³⁴

The biochemical parameters showed a lower percentage of patients with albumin, creatinine and serum urea levels below the reference values for HD patients when compared to other studies.

In a study conducted by Cavalcante et al.³⁵, the prevalence of 85.3% serum albumin <4.0 mg/dL was observed. This high prevalence of hypoalbuminemia, compared to the current study, can be justified by the higher cut-off point used in the Cavalcante et al.³⁵ study. The prevalence of hypoalbuminemia in Brazil varies from 15% to 85.3%, and there are several factors that trigger this difference in prevalence, as characteristics of the studied population and cut-off points of the hypoalbuminemia used by the HD centres³⁶. Appropriate rates of serum albumin are quite important for the chronic renal patient, since reduced levels of albumin are related to a worse prognosis and a greater risk of hospitalization in these patients³⁶.

A survey conducted between 2009 and 2010 in the state of Goiás showed that 56% of the patients studied had serum creatinine levels below that recommended for renal patients,³⁷ a very disturbing result different from the current study, where about 19.2% had serum creatinine reduced. In this study, the lower frequency of inadequacy of serum creatinine rates may demonstrate a certain adequacy of protein intake by patients.

Urea, in turn, also showed within its range for HD in most of the patients studied. Oliveira et al.³⁸ found a very similar result in their research. Urea levels may be influenced by factors such as protein ingestion or breakdown, and in dialysis patients, decreased rates of serum urea depend on the patient's residual renal function, and this is directly proportional to the mortality of these patients³⁹.

As for MIS, similar results were observed by Barros et al.⁴⁰ in 2014, who found an average MIS score of 4.0. A multicentre European study obtained a different result in their research, describing a mean MIS of 9.85⁴¹. Several factors, such as different dialysis protocols, population differences and different clinical conditions among the evaluated patients are

one of the causes that may justify this difference between the studies⁴⁰.

As it was observed with the biochemical indicators, the percentage of MIS inadequacy was considered low, indicating few patients at risk of presenting MIA syndrome. However, when MIS was associated with anthropometric and biochemical parameters, a moderate negative correlation was observed with BMI, WC, NC and creatinine, and a weak negative correlation with WHtR, suggesting that the making these anthropometric measurements may be a good alternative to identify and monitor the risk of nutrition associated with inflammation in these patients.

BMI correlated negatively with MIS, suggesting that the lower the BMI of a dialysis patient, the greater the risk of malnutrition and inflammation. However, in MIS, a BMI greater than 20 kg/m² does not score for nutritional risk, which may be an instrument bias, since it does not take into account the BMI range for the elderly population²⁰. BMI is a parameter widely used in clinical practice to classify the nutritional status of individuals and, despite its limitations, such as not differentiating between lean mass and fat mass, it is one of the most commonly performed in HD patients, since it is low cost, non-invasive and practical⁴².

Some authors report the relationship between a higher BMI and a good prognosis in CKD, since low weight is associated with higher mortality⁴³. Studies suggest that patients who perform HD should maintain their BMI > 23.0 kg/m² to ensure a positive impact on morbidity and mortality³⁸. Low weight and malnutrition are widely found among patients who perform HD. Factors such as dietary restriction, metabolic acidosis, protein catabolism and reduction of antioxidant capacity are involved in the presence of malnutrition and inflammatory process in patients with CKD on HD⁴⁴.

Regarding WC, NC and WHtR, it is known that these are indicators of visceral fat and their levels, when elevated, are associated with increased mortality due to the risk of cardiovascular diseases²⁷. However, levels that are much lower than the values recommended for WC and NC, since these measures are generally directly proportional to BMI, may be associated with malnutrition and, consequently, with the presence of inflammation.

The parameter that presented a better correlation with the MIS was serum creatinine. Several studies indicate the association of creatinine with the prog-

nosis of patients with CKD on HD⁴⁵. According to the literature, serum creatinine values below 10 mg/dL increase mortality of dialysis patients and may be related to malnutrition⁴⁶. Thus, it is important to routinely monitor serum creatinine levels in patients with CKD on HD, aiming at the rapid identification of patients with impaired nutritional status, to make a nutritional intervention adequately and precociously.

Demir et al.⁴⁷, in 2010, found a negative correlation between MIS and serum albumin ($r = -0.42$ and $p = 0.0001$). Some research suggests that the association between low serum albumin levels and elevated MIS increases mortality in patients with terminal CKD⁸. Thus, the presence of malnutrition, inflammation and reduction of serum albumin would lead to poor prognosis of the dialytic patient, causing an increase in oxidative stress and inflammatory markers, reinforcing the applicability of MIS as a clinical tool in the identification of inflammatory process in the dialysis stage of CKD⁴⁸.

The absence of a relationship between serum albumin and MIS suggests that the presence of malnutrition in these patients is type 1, in which the cause is related to low food intake (total energy), since the aetiology of malnutrition in patients with CKD on haemodialysis can be caused either by factors associated with food intake or by inflammatory factors⁴⁹.

The waist-to-hip ratio also did not prove to be a good parameter for the evaluation of the nutritional status and the presence of malnutrition and inflam-

mation of the patients on HD in this sample, since it did not present a correlation with the MIS.

The present study presented some limitations, such as the small sample number and the impossibility of evaluating PCR. However, in spite of the limitations, it was possible to obtain a significant result that should be further investigated, aiming at the adequate choice of the parameters used to evaluate the nutritional status of patients with CKD on HD. In addition, research with a design that allows studying the cause and effect of the events addressed should be carried out.

CONCLUSION

MIS presented a moderate negative correlation with BMI, WC, NC and creatinine, suggesting that these anthropometric and biochemical parameters can be used as indirect indicators of Malnutrition-Inflammation-Atherosclerosis syndrome in this series, particularly the serum creatinine that, among the studied parameters, was the indicator that presented the highest level of correlation and significance.

The applicability of MIS to clinical practice is quite important. This score had a moderate negative correlation with BMI, WC, NC and creatinine, suggesting that these anthropometric and biochemical parameters, particularly serum creatinine, can also be considered as an alternative to be used as an indirect indicator of MIA syndrome in this case, in a quick, simple and low cost manner.

RESUMO:

INTRODUÇÃO: A síndrome Desnutrição-Inflamação-Aterosclerose é frequente nos pacientes com doença renal crônica em hemodiálise, acarretando perda de proteínas corporais e produção de citocinas pró-inflamatórias.

OBJETIVO: Verificar, entre os indicadores nutricionais estudados, aqueles que melhor se correlacionam com a síndrome Desnutrição-Inflamação-Aterosclerose em pacientes submetidos à hemodiálise.

MÉTODOS: O estudo foi transversal, realizado na Clínica de Hemodiálise do Hospital Barão de Lucena, no Recife (PE), entre julho e agosto de 2016, com pacientes atendidos há pelo menos seis meses. Foram excluídos pacientes amputados, internados, com deficiência visual, cateter no pescoço, HIV positivo, ascite e/ou edema e aqueles incapazes de prestar informações no momento da entrevista. Os pacientes foram submetidos à avaliação antropométrica para a classificação do estado nutricional pela circunferência da cintura, perímetro do pescoço, índice de massa corporal, relação cintura-quadril e relação cintura-estatura. O estado nutricional relacionado à inflamação foi mensurado pelo escore Desnutrição-Inflamação e a avaliação do estado nutricional pelos indicadores bioquímicos: ureia, creatinina e albumina.

RESULTADOS: Participaram do estudo 27 indivíduos de ambos os sexos, adultos e idosos, com idade de $51,3 \pm 13,3$ anos. A avaliação antropométrica mostrou que a maior parte da população apresentava risco cardiovascular. A avaliação bioquímica relatou baixas frequências de desnutrição. Foi evidenciada síndrome Desnutrição-Inflamação-Aterosclerose em 3,7% dos pacientes. O escore Desnutrição-Inflamação apresentou correlação moderada negativa com o índice de massa corporal, circunferência da cintura, perímetro do pescoço, relação cintura-estatura e creatinina.

CONCLUSÃO: A correlação observada entre os parâmetros sugere que a maioria dos parâmetros avaliados pode ser utilizada como indicador indireto da síndrome Desnutrição-Inflamação-Aterosclerose.

PALAVRAS-CHAVE: Insuficiência renal crônica. Diálise renal. Desnutrição. Inflamação.

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