Renal Dysfunction and Inflammatory Markers in Hypertensive Patients seen in a University Hospital

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Abstract

Background: Today, chronic kidney diseases represent a great challenge to public health as regards the acquisition of knowledge to support interventions that can slow the progression of renal function loss.

Objective: To analyze the magnitude of the renal function deficit in hypertensive adult patients and its relationship with the following inflammatory markers: high-sensitivity C reactive protein, erythrocyte sedimentation rate, and neutrophil/lymphocyte ratio.

Methods: Cross-sectional study including 1,273 adult hypertensive patients of both genders, of whom 1,052 had renal function deficit, and 221 had no deficit, as diagnosed by the Modification of Diet in Renal Disease equation. The odds ratio (OR) and the prevalence ratio (PR) were used to determine the probability of the occurrence of inflammatory activity in renal disease.

Results: Renal function deficit was diagnosed in 82.6% of the patients assessed, and most of the sample (70.8%) was classified as in stage 2 of chronic kidney disease. In the regression model, metabolic syndrome ($PR_{adjusted}$ = 1.09 [95%CI: 1.04-1.14]), high-sensitivity C reactive protein ($PR_{adjusted}$ = 1.54 [95%CI: 1.40-1.69]) and erythrocyte sedimentation rate ($PR_{adjusted}$ = 1.20 [95%CI: 1.12-1.28]) remained independently associated with the renal function deficit. However, considering the individuals classified as in stage 2 of renal function deficit, the chance of abnormalities in inflammatory markers were OR = 10.25 (95%CI: 7.00-15.05) for high-sensitivity C reactive protein, OR = 8.50 (95%CI: 5.70-12.71) for neutrophil/lymphocyte ratio, and OR = 7.18 (95%CI: 4.87-10.61) for erythrocyte sedimentation rate.

Conclusion: The results show an association of inflammatory activity and metabolic syndrome with renal function deficit (Arq Bras Cardiol. 2013;100(6):538-545).

Keywords: Hypertension; Kidney Diseases; Inflammation; Metabolic Syndrome.

Introduction

Changes in the profile of mortality and morbidity in the world population have shown an increase in the incidence of chronic kidney disease (CKD), which is considered one of the major challenges to public health in this century, with all its economic and social implications[1]. According to criteria of the National Kidney Foundation/Kidney Disease Outcomes Quality Initiative[2], CKD is defined as a damage in the renal parenchyma and/or decreased glomerular filtration rate (GFR) for a period equal to or longer than three months, as manifested by markers of kidney damage, including abnormalities in blood/urine, imaging tests or pathological studies[2]. In the United States of America, Europe and Asia, 11% to 33% of the general population are estimated to have CKD, most of them in the initial stages of the disease[3].

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According to the literature, systemic hypertension (SH) associated with CKD increases the cardiovascular risk and, as the renal dysfunction progresses, the prevalence of SH also increases, affecting approximately 90% of patients with kidney diseases. Therefore, the detection, treatment and control of SH are key measures to reduce the incidence of renal and cardiovascular events[2,4,5].

Like CKD, hypertension also reflects a state of endothelial inflammation[5]. According to the European and Japanese recommendations, the use of inflammation markers such as high-sensitivity C reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR) and the neutrophil/lymphocyte ratio (N/L R) in patients with CKD improves the diagnosis and treatment, thus reducing the cardiovascular mortality[6,7].

In Brazil, there are few studies on the relationship between CKD and the inflammatory markers hs-CRP, N/L R, and ESR. According to several authors, both hs-CRP and ESR can be used in the identification of CKD, increasing the sensitivity and specificity of this diagnosis[7-9]. Kocyigit et al[10] reported that a N/L R < 1 may be indicative of an underlying inflammatory state and predict the progression rate of stage-4 CKD, thus indicating the need for a dialysis procedure.

Thus, the objective of this study was to analyze the magnitude of renal dysfunction and its relationship with three potential inflammatory markers (hs-CRP, N/L R, and ESR) used in the clinical practice, in hypertensive patients.

Methods

Study design and sample

Cross-sectional analytical study including 2,122 hypertensive patients of both genders followed up for four years in the Hypertension Clinic of the Clinics Hospital of the Federal University of Pernambuco. Patients with secondary hypertension (n = 5), cardiac arrhythmias (n = 26), heart failure (n = 7), previous myocardial infarction (n = 9), dyslipidemias in use of lipid-lowering medication (n = 46), diabetes mellitus (n = 203), and those with incomplete information in their medical records (n = 553) were excluded from the study. The final sample size was of 1,273 patients. The antihypertensive treatment regimen of all patients included 1-4 drugs (betablocker, hydrochlorothiazide, angiotensin-converting-enzyme inhibitor, calcium-channel blocker, hydralazine, methyldopa).

The glomerular filtration rate (GFR) was estimated according to criteria of the National Kidney Foundation/ Kidney Disease Outcomes Quality Initiative[2], using the equation proposed by Levey et al[11]. The renal function deficit (RFD) was defined as a GFR ≤ 89 mL/min/1.73m^2 and classified in five stages: 1 – GFR ≥ 90 mL / min/1.73m^2; 2 – GRF = 60-89.9 mL / min/1.73m^2; 3 – GRF = 30-59.9 mL / min/1.73m^2; 4 – GRF = 15-29.9 mL/ min/1.73m^2; 5 – GRF < 15 mL/min/1.73m^2. Patients in stages 2, 3, and 4 were considered as having RFD. Patients in stage 1 were considered as not having renal function deficit[2].

Study variables

The variables considered were: sociodemographic variables (age, gender and level of education), laboratory variables (hs-CRP, ESD, and N/L R), anthropometric variables (body mass index – BMI, and waist circumference – WC), and clinical variables (metabolic syndrome – MS, and systemic hypertension – SH).

All participants received information on the objectives of the study and, after giving written informed consent, they replied to a questionnaire with socioeconomic, demographic and clinical information. Also, anthropometric measurements were taken and a blood sample was collected for laboratory evaluation.

The level of education was assessed in terms of years of schooling, and the sample was stratified in < 4 years and ≥ 4 years. Hs-CRP levels were determined using the Cobas C 501 Automated method, considering values < 0.5 mg/dL as normal reference values, for both men and women. For the assessment of first-hour ESR, the capillary photometry method was used, with normal reference values ranging from 0-15 mm for men, and 0-20 mm for women, and the cut-off point in the upper limits of normal. N/L R inversion, on blood count, was assessed using the ABX Pentra DX 120 method, with slide review, and was considered abnormal for values > 1.

Weight and height were measured according to the techniques recommended[12]. Weight was measured using a Filizola® model scale, with 150-kg capacity, and height was measured using an 1.90m-capacity anthropometer connected to the scale. The diagnosis of excess weight was based on the BMI, as classified according to the cut-off points of the World Health Organization (WHO), considering excess weight as BMI ≥ 25 kg/m^2[2,13]. The classification proposed by Lipschitz[14] was used for elderly individuals, with the cut-off point of BMI ≥ 27 kg/m^2. The WC was measured at the midpoint between the lower rib and the iliac crest, using a flexible non-stretchable tape measure without compressing the underlying tissues, with the patient in the standing position, relaxed abdomen, arms along the body and feet together. The cut-off points for increased waist circumference were ≥ 94 cm (men) and ≥ 80 cm (women)[13].

Blood pressure (BP) was measured using the auscultatory method, with a Takaoka model 203 mercury-column sphygmomanometer duly calibrated and a Littmann stethoscope, according to the technique recommended. The BP measurements considered were those taken in the first visit and with the patients not taking any antihypertensive medication. The classification of hypertension followed the recommendations of the VI Brazilian Guidelines of Hypertension[4].

MS was identified according to criteria of the International Diabetes Federation (IDF)[15], and was based on the presence of abdominal obesity (waist circumference ≥ 94 cm for men, and ≥ 80 cm for women), associated with at least two of the following factors: high density lipoprotein (HDL - cholesterol) < 40 mg/dL for men, and < 50 mg / dL for women; triglycerides ≥ 150 mg/dL; fasting blood glucose ≥ 100 mg/dL; SH, as classified according to the VI Brazilian Guidelines of Hypertension[4].

Data analysis and processing

The construction of the data bank and statistical analysis were carried out using the Epi-info version 6.04 and SPSS version 13.0 software programs. Data were double-entered and verified with Validate, in order to check their consistency and validation. Data were described as medians + interquartile intervals for continuous variables. Proportions were used to express dichotomous variables. The best adjustment for normal distribution was assessed using the Kolmogorov-Smirnov test.

The influence of the risk factors studied on renal function was analyzed using the Poisson regression model. Variables with significance ≤ 0.20 in the non-adjusted bivariate analysis were considered in the composition of the model, and those not meeting this definition were also included in the model because of their clinical relevance (MS). The stepwise method (variable selection by steps) with backward elimination was used in the adjusted analysis. Only variables associated with a p value < 0.05 remained in the final model. The tests analyzed were applied with a 95% confidence interval and 5% significance level.

In order to verify the existence of an association between renal dysfunction and the markers selected, the chi-square test with Yates correction or Fisher's exact test were used; when

criteria for the application of these tests were not met, the Mann-Whitney U test was used. The strength of association was assessed by the prevalence ratio (PR) and odds ratio (OR), considering a 95% confidence interval.

Ethical aspects

The project was approved by the Research Ethics Committee involving Humans, of the Health Sciences Center of the Federal University of Pernambuco (CEP/CCS/UFPE), record CEP/CCS/UFPE no. 343/09 and SISNEP FR – 300564, according to Resolution no. 196/96 of the National Heath Council.

Results

Most of the 1273 hypertensive patients included in the study were females (73.1%, 95%CI: 0.95-1.07). The median systolic blood pressure (SBP) was 138 mmHg; the median diastolic blood pressure (DBP) was 86 mmHg; and the median age was 59 [interquartile interval (IQ): 52-67], with minimum age of 41 and maximum of 92 years. Approximately 60% of patients were on a combination of two drugs, whereas 12% were on 3-4 medications. RFD was diagnosed in 82.6% of the patients assessed, and most of the sample (70.8%) was on stage-2 CKD. Moderate deficit (stage 3) was observed in 28.2% of patients, whereas significant renal damage (stage 4) associated with signs and symptoms of uremia was observed in approximately 1% of patients; no stage 5 cases were observed.

RFD was more frequent as age increased ($p < 0.05$), with a 1.22 risk in the elderly in comparison to adults; in females, the risk was 1.07 higher than in males. Patients with a lower level of education showed a higher risk for reduced GFR (PR = 1.10, 95%CI: 1.04-1.17). In relation to SH, individuals with systolic hypertension alone showed a 15% higher chance of having RFD when compared to stage-2 patients. Inflammatory markers were associated with RFD, especially in individuals with high hs-CRP. As regards MS and anthropometric variables, no statistically significant associations with RFD were found (Table 1).

Table 2 shows that, after adjustment for potential risk factors for RFD, only three variables remained in the model, demonstrating an independent association with RFD; increased hs-CRP was the factor more strongly associated with the occurrence of RFD (adjusted PR = 1.54, 95%CI: 1.40-1.69).

All inflammatory markers, alone or combined, showed a statistically significant association with RFD, although the levels of inflammatory markers in individuals with RFD were within the limits of normal (Table 3).

In relation to the inflammatory markers, hs-CRP was more prevalent in the initial phase of the disease (stage 2), with a 10.25 (95%CI: 7.00-15.05) higher chance of being abnormal in the comparison between stages 2 and 1 of RFD (Table 4).

Comparisons of levels of inflammatory markers in the different RFD stages are shown in Table 5. ESR and hs-CRP levels increased with the progression of RFD in the individuals studied.

Discussion

In Brazil, studies on the prevalence of abnormalities of inflammatory markers in chronic kidney diseases are still scarce. It is important to point out that, although our study population comprised patients seen in a hypertension outpatient clinic, with individuals classified in different SH stages and showing mainly systolic hypertension alone, the absence of patients with RFD in the end-stage kidney disease (stage 5) and the small number of patients (10 individuals) in stage 4 may be attributed to the fact that the hypertensive process was controlled, probably because of the multidisciplinary approach provided by the clinic[16,17].

The fact that approximately 70% of patients had their blood pressure controlled using 2-3 different classes of antihypertensive drugs is not surprising. A possible explanation for this finding could be the small percentage of compliance to lifestyle changes observed in all hypertension programs, even those with a disciplinary character. It is true that the growing frequency of use of antihypertensive drug combinations and effective compliance to these medications on a regular and continuous basis tend to provide a better control of hypertension. It is important to point out that, in the present study, approximately 48% of the study population was classified as having stage-3 SH, and 46.9% were 60 years old or older, two conditions which are favorable to cardiovascular diseases; the percentage of 70% of patients using 2-3 drugs, in this case, reflects the great and significant blood pressure control in that group undergoing multidisciplinary care.

The high prevalence of RFD found in this study is a matter of concern, especially because its occurrence is associated with changes in inflammatory biomarkers. The inflammatory process is known to be highly prevalent in patients with CKD; also, it is associated with cardiovascular morbidity and mortality, and the rates of clinical events (obesity and dyslipidemias) found in the present study could explain the decline in renal function and activation of the acute- or chronic-phase inflammatory response. Our findings corroborate those of Shankar et al[18], who studied 4926 patients to investigate the relationship between several inflammatory biomarkers, including hs-CRP, and the risk of developing CKD; the authors found a positive and independent association, thus predicting the risk of developing this condition.

The association found between a low level of education and RFD is in accordance with the literature. The findings of this study may reflect a difficulty to understand which would contribute to the non-compliance to treatment of the disease. The higher prevalence of the female gender confirms the greater longevity of women, an aspect that was also observed in other studies[19-21,22].

One fact that stands out is the high frequency of abnormal hs-CRP among the markers studied. The acute phase inflammatory proteins are so called because their levels are higher in this inflammation phase; however, they continue to be produced, albeit at lower levels, in chronic persistent inflammations. In very recent studies, chronic inflammation has been pointed as a risk factor and treatment target for CKD,

Table 1 - Demographic, socioeconomic, clinical and anthropometric characteristics of hypertensive patients with and without renal deficit seen in a university hospital. Pernambuco, Brazil, 2011

Variables	Renal Function Deficit		Total	Prevalence ratio	95%CI*	†p value
	YES (1,052)	NO (221)	N = 1,273			
	n (%)	n (%)	N (%)			
Gender						
Female	783 (84.1)	148 (15.9)	931 (73.1)	1.07	1.01-1.14	0.028
Male	269 (78.7)	73 (21.3)	342 (26.9)	1.00		
Age (years)						
≥ 60	546 (91.5)	51 (8.5)	597 (46.9)	1.22	1.16-1.28	< 0.001
< 60	506 (74.9)	170 (25.1)	676 (53.1)	1.00		
Level of education (years of schooling)						
< 4 years	715 (85.3)	123 (14.7)	838 (65.8)	1.10	1.04-1.17	0.001
≥ 4 years	337 (77.5)	98 (22.5)	435 (34.2)	1.00		
SH‡ Class						
Systolic hypertension alone	102 (89.5)	12 (10.5)	114 (9.0)	1.15	1.06-1.24	0.008
Stage 3	518 (85.5)	88 (14.5)	606 (47.6)	1.09	1.04-1.16	0.001
Stage 2	432 (78.1)	121 (21.9)	553 (43.4)	1.00		
Excess weight						
Yes	771 (81.5)	175 (18.5)	946 (74.3)	0.95	0.90-1.00	0.082
No	281 (85.9)	46 (14.1)	327 (25.7)	1.00		
Abnormal waist circumference§						
Yes	834 (82.5)	177 (17.5)	1011 (79.4)	0.99	0.93-1.05	0.857
No	218 (83.2)	44 (16.8)	262 (20.6)	1.00		
Metabolic syndrome						
Yes	756 (83.4)	150 (16.6)	906 (71.2)	1.03	0.98-1.10	0.268
No	296 (80.7)	71 (19.3)	367 (28.8)	1.00		
High-sensitivity C reactive protein						
Abnormal	834(95.0)	44 (5.0)	878 (69.0)	1.72	1.57-1.88	< 0.001
Normal	218(55.2)	177 (44.8)	395 (31.0)	1.00		
Erythrocyte sedimentation rate						
Abnormal	753 (95.0)	40 (5.0)	793 (62.3)	1.52	1.42-1.64	< 0.001
Normal	299 (62.3)	181 (37.7)	480 (37.7)	1.00		
Neutrophil/lymphocyte ratio						
Abnormal	766 (95.4)	37 (4.6)	803 (63.1)	1.57	1.46-1.69	< 0.001
Normal	286 (60.9)	184 (39.1)	470 (36.9)	1.00		

**CI: confidence interval. † p value: Chi-square test. ‡SH class: classification of systemic hypertension (BGH VI, 2010). Systolic hypertension alone: ≥ 140 and < 90mmHg. Stage 3: ≥ 180 and/or ≥ 110 mmHg. Stage 2: 60-89.9 min/mL. §Waist circumference ≥ 94cm for men and ≥ 80cm for women.*

and, among several inflammatory biomarkers, hs-CRP has been shown to independently predict mortality in patients with CKD[23-25]. There are multiple causes for the highly prevalent state of inflammation in CKD. These causes are not yet fully understood, and seem to include, among other factors, volume overload, comorbidities, clinical events, metabolic and genetic factors, as well as the renal disease per se with its different etiopathogenic inter-relations[26].

Plasma levels of fibrinogen which, when elevated, are able to trigger an increase in ESR, have also been suggested as cardiovascular disease markers[27]. In the clinical practice, because ESR determination is a simple and low-cost test, it is commonly used as an unspecific marker of pathological conditions. Collares and Vidigal[28] reported that physiological conditions such as gender and age, and pathological conditions such as chronic inflammatory processes, chronic renal failure,

Table 2 - Association between renal function deficit and potential risk factors, prevalence ratio (PR) adjusted* for chronic kidney disease in hypertensive patients seen in a university hospital. Pernambuco, Brazil, 2011

Variables	PR† (adjusted)	95%CI‡ (PR†)	p value§
Metabolic syndrome			**0.001**
Yes	1.09	1.04-1.14	
No	1.00	-	
Erythrocyte sedimentation rate			**< 0.001**
Abnormal	1.20	1.12-1.28	
Normal	1.00	-	
High-sensitivity C reactive protein			**< 0.001**
Abnormal	1.54	1.40-1.69	
Normal	1.00	-	

**Poisson regression: model adjusted for the renal function deficit. †PR: prevalence ratio. ‡CI: confidence interval. §p value: chi-square test.*

Table 3 - Association between inflammatory markers alone or in combination and renal function deficit in hypertensive patients seen in a university hospital. Pernambuco, Brazil, 2011

Inflammatory markers	Renal function deficit				Total		p value*
	YES		NO				
	N = 1052	%	N = 221	%	N = 1273	%	
hsCRP†							
Abnormal	834	(95.0)	44	(5.0)	878	(69.0)	< 0.001
Normal	218	(55.2)	177	(44.8)	395	(31.0)	
N/L R‡							
Abnormal	766	(95.4)	37	(4.6)	803	(63.1)	< 0.001
Normal	286	(60.9)	184	(39.1)	470	(36.9)	
ESR§							
Abnormal	753	(95.0)	40	(5.0)	793	(62.3)	< 0.001
Normal	299	(62.3)	181	(37.7)	480	(37.7)	
hsCRP + ESR							
Abnormal	686	(96.2)	27	(3.8)	713	(56.0)	< 0.001
Normal	366	(65.4)	194	(34.6)	560	(44.0)	
hsCRP + ESR + N/L R							
Abnormal	705	(95.9)	30	(4.1)	735	(57.7)	< 0.001
Normal	347	(64.5)	191	(35.5)	538	(42.3)	
ESR + N/L R							
Abnormal	743	(95.9)	32	(4.1)	775	(60.9)	< 0.001
Normal	309	(62.0)	189	(38.0)	498	(39.1)	
hsCRP + N/L R							
Abnormal	686	(96.2)	27	(3.8)	713	(56.0)	< 0.001
Normal	366	(65.4)	194	(34.6)	560	(44.0)	

** p value: chi-square test. †hsCRP: high-sensitivity C reactive protein. ‡N/L R: segmented neutrophils/typical lymphocytes ratio. §ESR: erythrocyte sedimentation rate.*

Table 4 - Odds ratio (95%CI) of marker levels in the different stages of renal function in hypertensive patients seen in a university hospital. Pernambuco, Brazil, 2011

Characteristic	N (%)	Renal Function Stage 1	2	3	4
	1,273	N = 221	N = 745 (1,052)	N = 297 (1,052)	N = 10 (1,052)
High-sensitivity C reactive protein					
Normal	395 (31.0)	177 (44.8)	210 (53.2)	8 (2.0)	0 (0.0)
Abnormal	878 (69.0)	44 (5.0)	535 (60.9)	289 (32.9)	10 (1.1)
OR* (95%CI†)			10.25 (7.00-15.05)		
Neutrophil/lymphocyte ratio					
Normal	470 (36.9)	184 (39.1)	275 (58.6)	11 (2.3)	0 (0.0)
Abnormal	803 (63.1)	37 (4.6)	470 (58.6)	286 (35.6)	10 (1.2)
OR (95%CI)			8.50 (5.70-12.71)		
Erythrocyte sedimentation rate					
Normal	480 (37.7)	181 (37.7)	288 (60.0)	11 (2.3)	0 (0.0)
Abnormal	793 (62.3)	40 (5.0)	457 (57.6)	286 (36.1)	10 (1.3)
OR(95%CI)			7.18 (4.87-10.61)		

**OR: odds ratio. †CI: confidence interval.*

Table 5 - Stages of renal function deficit according to the levels of inflammatory markers in hypertensive patients seen in a university hospital. Pernambuco, Brazil, 2011

Inflammatory markers	Stage of Renal Function Deficit (N = 1,273)				
	1 (221)	2 (745)	3 (297)	4 (10)	
	Med* (IQ)†	Med (IQ)	Med (IQ)	Med (IQ)	p value†
High-sensitivity C reactive protein	0.46	0.78	1.69	2.46	< 0.001[a]
	(0.40;0.49)	(0.49;1.02)	(1.08;2.38)	(1.35;3.24)	
Neutrophil/lymphocyte ratio	1.87	0.84	0.58	0.37	< 0.001[b]
	(1.24;2.37)	(0.60-1.25)	(0.43;0.76)	(0.31;0.45)	
Erythrocyte sedimentation rate	16.00	27.00	44.00	49.50	< 0.001[c]
	(14.00;19.00)	(19.00;37.00)	(35.00;52.00)	(46.8;57.75)	

**Med: median. †IQ: interquatile interval. †p value, Mann-Whitney U test for non-paired variables [a,b,c].*

diabetes mellitus, obesity, infections, anemia, neoplasms, tissue damage (acute myocardial infarction, stroke) and connective tissue diseases increase ESR values[28].

The high prevalence of MS and the fact that it remained in the model after adjustment by Poisson regression show a strong independent association with RFD along with hs-CRP and ESR. A possible explanation would be the fact that, in our study sample, all individuals were hypertensive, with an associated high prevalence of abnormal WC, which are two components of MS. Our findings corroborate those of the literature[29].

MS has emerged as an important predictor of metabolic complications, with resulting adverse health effects, and is not only related to an increased cardiovascular and metabolic risk in elderly individuals but also presents as a well established predisposing factor for vascular diseases, especially atherosclerosis and SH[23]. Prospective studies have demonstrated that MS and inflammation have synergistic and additive effects in atherosclerotic processes[30,31]. Conversely, inflammation has been involved in the pathogenesis of MS, especially as a mechanism of insulin resistance[31]. Ridker et al[30] found a significant association between high hs-CRP levels and prediction of MS, as well as an increased risk for cardiovascular diseases (CVD). In epidemiological studies, MS has also been pointed as a risk factor for the development of CKD[29,32,33]. Lee et al[29] investigated the relationship between hs-CRP, MS, and CKD in 9586 individuals without diabetes mellitus or SH and found an association of MS and high hs-CRP levels with an increased prevalence of CKD[29].

The high prevalence of inflammatory markers, alone or in combination, in our study sample is a well established finding in the literature, showing that the elements of a chronic inflammation seem to permeate the hypertensive renal disease, thus more objectively contributing to the renal arteriolar degenerative process[34].

The finding of a high frequency of patients with renal damage and mild decrease in the renal function not progressing to more severe stages of the disease could be explained by the systematic follow-up of these patients by a multidisciplinary team. This would help keep the blood pressure levels of most of these patients within adequate limits, thus preventing or reducing target-organ damage, which is common in hypertensive individuals. Based on these data, we can suggest that it is possible to correlate hypertensive patients with chronic renal failure, therefore affected by arteriolar abnormalities, with the presence of a common etiologic factor, possibly the persistent and chronic inflammation, as expressed by hs-CRP, N/L R and ESR, which are markers of acute or chronic inflammatory processes.

Some aspects could be considered as study limitations. The first is the study design used, considering that the follow-up period (four years) would facilitate the inclusion, in the study population, of individuals with history of hypertension in different phases (initial, intermediary, and advanced), which could influence the levels of inflammatory markers. The second is that we did not use a control group (non-hypertensive patients), paired by gender and age, to verify the association between dependent / independent variables. However, for operational reasons, even with the strict methodology used in data collection a control group could not be included.

Although an increase in cardiovascular mortality can only be demonstrated in longitudinal studies, the parameters analyzed here in a cross-sectional study suggest that the determination of hs-CRP levels (already known as an important cardiovascular risk marker), ESR, and microalbuminura be included as a routine in the screening process of hypertensive patients seen in public health services to detect early kidney disease. In the clinical practice, these tests, in association with the assessment of the components of MS, could provide an early detection of increased CVD risk in this population, at a lower operational cost and with a multidisciplinary approach by the professionals involved.

Conclusion

The results show an association of inflammatory activity and metabolic syndrome with renal function deficit.

Author contributions

Conception and design of the research: Braga FLM, Arruda IKG, Diniz AS, Braga MDM, Chaves Júnior HC; Acquisition of data: Braga FLM, Arruda IKG; Analysis and interpretation of the data, Writing of the manuscript and Critical revision of the manuscript for intellectual content: Braga FLM, Arruda IKG, Diniz AS, Cabral PC, Lemos MCC, Braga MDM, Chaves Júnior HC; Statistical analysis: Diniz AS, Chaves Júnior HC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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