Systemic Hypertension and Microalbuminuria

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Summary

Objetivo: To identify the prevalence of microalbuminuria and target organ lesions and their association in a hypertensive population undergoing treatment.

Methods: This observational, descriptive and cross-sectional study was conducted between April and August 2006, and included 153 hypertensive patients undergoing treatment at the Internal Medicine and Cardiology Outpatient Clinics at a University Hospital in the Southern Region of Brazil.

Results: This observational, descriptive and cross-sectional study was conducted between April and August 2006, and included 153 hypertensive patients undergoing treatment at the Internal Medicine and Cardiology Outpatient Clinics at a University Hospital in the Southern Region of Brazil.

Conclusion: The prevalence of microalbuminuria in the study population was 13.7% and that of target organ lesions was 48.4%; a statistically significant association was found. Microalbuminuria is also associated with cardiac lesions, including in the geriatric population. (Arq Bras Cardiol 2007;89(6):376-381)

Key words: Hypertension; albuminuria; target organs; risk factors.

Introduction

Systemic hypertension (SH) is currently defined as systolic blood pressure (SBP) greater than or equal to 140 mmHg and/or diastolic blood pressure (DBP) greater than or equal to 90 mmHg in adults 18 years of age or older[1-4]. Throughout time this classification has been modified, as new studies evaluate patient evolution in accordance with blood pressure levels.

Great importance has been given to microalbuminuria as a prognostic marker of cardiovascular and/or renal risk in diabetics[5,6], hypertensives[6-10] and the population as a whole[11-13]. Studies have demonstrated an ongoing association of microalbuminuria with cardiovascular events and kidney lesions, that is, the higher the urinary albumin excretion the greater the risk to develop these conditions[14].

Microalbuminuria is defined as elevated urinary albumin excretion, exceeding normal levels without reaching the minimum levels that can be detected by routine laboratory methods, that is, an albumin excretion between 30 and 300 milligrams in 24 hours[5,15-17]. These cut-off points were defined based on studies that show the risk curve to develop nephropathy in diabetic patients[18], and has been questioned by some authors[12,19-21].

The mechanism that causes increased urinary albumin excretion is not well defined, and the reasons why this excretion is associated with increased cardiovascular risk have not yet been established. The prevailing explanation is that microalbuminuria represents a generalized dysfunction of vascular endothelium, increasing permeability and causing the leakage of albumin through the glomerular membrane[17,18,22].

Even though there are disparities between the various studies, the prevalence of microalbuminuria generally ranges between 20% and 30% in untreated hypertensive patients and is as high as 25% in patients undergoing anti-hypertensive treatment[7,8,10,23].

Owing to the importance of the risk factors when assessing SH patients and the prognostic value attributed to microalbuminuria, the objective of the present study is to identify the prevalence of microalbuminuria and the association between this risk marker and target organ lesions, in a population of hypertensive patients undergoing anti-hypertensive treatment.

Method

An observational, descriptive and cross-sectional study was conducted at the Internal Medicine Outpatient Healthcare Center and the Cardiology Outpatient Clinic at a University Hospital in the Southern Region of Brazil, between April and August 2006.

The medical charts of the patients were reviewed in order to select SH patients that had not been diagnosed with diabetes mellitus, and when they arrived for their previously scheduled consultations at the abovementioned outpatient clinics, they were invited for an interview. Therefore, from the 201 patients that agreed to participate in the study, 153 met the inclusion criteria, comprising the final sample.

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Patients with essential SH, undergoing anti-hypertensive treatment, from both genders, 18 years of age or older, who agreed to participate in the study and supplied an isolated early morning urine sample were included in the study. Patients with clinical and/or laboratory evidence of secondary SH, a diagnosis of diabetes mellitus and chronic kidney disease were excluded from the study. Patients who presented a partial urine test with signs of urinary tract infection or proteinuria were also excluded.

The following variables were evaluated: age, gender, race, body mass index (BMI), smoking, sedentary lifestyle, presence of target organ lesions and cardiovascular disease, lipid profile, blood pressure levels, SH duration, and presence of microalbuminuria. The patients were divided into two groups based on age: geriatrics (60 years or older) and non-geriatrics (younger than 60 years).

A ratio between the concentration of albumin and urinary creatinine within an interval of 30 to 300 milligrams of albumin per gram of creatinine was considered positive for microalbuminuria. The albuminuria assay was conducted using the nephelometry technique (Behring Nephelometer 100, Dade Behring®) and urinary creatinine was measured using the Jaffe technique. After proper unit conversions, the albumin/creatinine ratio was obtained, except when the urinary albumin concentration was less than 12mg/l (lowest equipment detection limit).

This study was approved by the University's Human Research Ethics Committee. All the patients signed a free and informed consent form.

The data were analyzed using the program Epi Info® v.6.04. The chi-square test (χ^2) was used to compare variable prevalence between the groups, using a confidence interval of 95% ($p<0.05$). The F-statistics variance analysis was used to compare the mean values between the groups, with the same confidence interval.

Results

Between April and August 2006, 201 patients from the Internal Medicine Outpatient Healthcare Center and the Cardiology Outpatient Clinic at a University Hospital were interviewed; 153 met the inclusion criteria. From these, 21 presented microalbuminuria (13.7%).

The normoalbuminuria and microalbuminuria groups were similar, with a predominance of females [91/132 (68.9%) *versus* 12/21 (57.1%)], white race [116/132 (87.8%) *versus* 18/21 (85.7%)] and a mean age of 60.7±13 years for the patients with normoalbuminuria and 63.9±12.7 for those with microalbuminuria (Table 1).

In relation to clinical characteristics, smoking [29.5% (39/132) *versus* 28.6% (6/21)], sedentary lifestyle [59.1% (78/132) *versus* 47.6% (10/21)] and obesity [31.8% (42/132) *versus* 23.8% (5/21)] were more prevalent in the normoalbuminuria group, while dyslipidemia was more prevalent in the microalbuminuria group [52.4% (11/21) *versus* 34.8% (46/132)] (Table 2). In relation to lipid levels, a statistically significant difference was only found for HDL cholesterol (46.0±12.9 mg/dl for those with normoalbuminuria *versus* 39.7±10.2 mg/dl for those with microalbuminuria; $p=0.03$)

The two groups were similar in relation to SBP (143.3±18.3 mmHg *versus* 142.5±21.5 mmHg), DBP (88.0±12.0 mmHg *versus* 86.2±10.7 mmHg) and SH duration (116.3±104.4 months *versus* 114.9±139.6 months) (Table 2).

The prevalence of at least one target organ lesion was 48.4% (74/153) in the general population, and was greater in the microalbuminuria group [76.2% (16/21) *versus* 43.9% (58/132) in the normoalbuminuria patients], which was statistically significant ($p=0.006$) (Table 3).

The most common lesions presented by the study patients were cardiac [41.8% (64/153)] particularly angina and/or acute myocardial infarction (AMI) [41/153 (26.8%)] and left ventricular hypertrophy (LVH) [21/153 (13.7%)] followed by congestive heart failure (CHF) [17/153 (11.1%)]. Encephalitic stroke (ES) or transient ischemic attack (TIA) [10/153 (6.5%)]; peripheral arterial disease [10/153 (6.5%)] and hypertensive retinopathy [2/153 (1.3%)] were less prevalent (Table 3).

A statistically significant association was found between cardiac lesions and microalbuminuria ($p=0.003$) which were presented by 71.4% (15/21) of the patients, while only 37.1% (49/132) of the normoalbuminuria patients presented this type of lesion (Table 3).

Half of the study population was comprised by the geriatric group [51% (78/153)] and the other half by the non-geriatric group [49% (75/153)] with a similar microalbuminuria prevalence in both groups [15.4% (12/78) *versus* 12.0% (9/75)] (Table 4).

There was a statistically significant association ($p=0.006$) between the presence of microalbuminuria and cardiac lesions in the geriatric group; however, this was not found in the non-geriatric group (Table 5). Using logistic regression analysis, we observed that the microalbuminuria, and not age, has the greatest association with cardiac lesions ($p=0.005$) (Table 6).

Discussion

Systemic hypertension and its complications are responsible for a large portion of the hospital admissions in Brazil, representing a very high socioeconomic cost. During 2003, cardiovascular diseases were responsible for 27.4% of the deaths in the country, with a direct relation between cardiovascular mortality and blood pressure levels[2].

Considering that roughly 20% to 40% of the Brazilian population have blood pressure levels greater than or equal to 140 per 90 mmHG[1,2], the importance of this relationship and the necessity to study factors related to it is recognized.

Microalbuminuria was initially defined as a urinary albumin excretion value that would be related to a greater risk to develop nephropathy in diabetic patients[18]. Studies conducted later demonstrated that microalbuminuria is also associated with worse cardiovascular outcomes, even in the general population[18,24]. Although the mechanism is still not clear, it is believed to be a renal indication of a generalized disorder of vascular endothelium with permeability alterations[17,18,22].

Table 1 – Demographic Profile – Hypertensive patients undergoing treatment and microalbuminuria

	Group NA (n = 132)	Group MA (n = 21)	Total (n = 153)	p*
Female Gender (%)	91 (68.9)	12 (57.1)	103 (67.3)	0.28
White (%)	116 (87.8)	18 (85.7)	134 (87.6)	0.72
Age ± SD	60.7 ± 13.0	63.9 ± 12.7	61.1 ± 13	0.29

*NA – normoalbuminuria; MA – microalbuminuria; SD – standard deviation ; *: The analyses conducted were the chi-square test for proportion analysis and the F test for variance analysis.*

Table 2 – Clinical Profile – Hypertensive patients undergoing treatment and microalbuminuria

	Group NA (n = 132)	Group MA (n = 21)	Total (n = 153)	p*
Smoking (%)	39 (29.5)	6 (28.6)	45 (29.4)	0.92
Sedentary lifestyle (%)	78 (59.1)	10 (47.6)	88 (57.5)	0.32
Obesity (%)	42 (31.8)	5 (23.8)	47 (30.7)	0.46
Dyslipidemia (%)	46 (34.8)	11 (52.4)	57 (37.2)	0.12
SBP ± SD	143.3±18.3	142.5±21.5	143.2±18.7	0.85
DBP ± SD	88.0±12.0	86.2±10.7	87.7±11.8	0.52
SH duration, months ± SD	116.3±104.4	114.9±139.6	116.1±109.3	0.95

*NA – normoalbuminuria; MA – microalbuminuria; SD – standard deviation; SBP – systolic blood pressure; DBP – diastolic blood pressure; SH – systemic hypertension; *: The analyses conducted were the chi-square test for proportion analysis and the F test for variance analysis.*

Since the relation between microalbuminuria and a worse cardiovascular prognosis has been established, various authors have tried to determine the variables associated with it, in order to define a profile of high risk patients and the possible strategies to prevent or diminish the progression to kidney disease and cardiovascular events.

First, we should remember that there are individual variations in urinary albumin excretion during the day and on different days. Therefore, the diagnosis of microalbuminuria should only be established when two of three samples of first morning urine present an altered albumin/creatinine ratio[16,24,25].

Among the factors that can cause transitory increases of urinary albumin excretion are overtiring physical exertion, urinary tract infection, decompensated heart failure, acute febrile diseases and vaginal secretions[24-26]. Blood pressure elevations during pregnancy or the development of gestational diabetes also cause significant increases in albuminuria[26]. These factors should be considered in the evaluation of the test results.

Some studies demonstrate associations between microalbuminuria and gender, race, age, blood pressure levels, cholesterol fractions, smoking and BMI[19,27]; however, in the majority of the studies there is a great deal of controversy in regard to study variables.

For example, Agrawal et al[8] demonstrated an association with age, male gender, SH duration, treatment duration and blood pressure levels, whereas Nakamura and associates[10], Clausen et al[11] and Redon et al[28] did not observe this relationship.

Three other studies with untreated hypertensive patients also present conflicting results. Palatini et al[29] did not observe a relation with smoking, physical activity, BMI, age, family history of early onset cardiovascular disease or SH duration, whereas Leoncini et al[30] found an association with age, BMI, smoking, HDL cholesterol, triglycerides and blood pressure levels. Pontremoli et al[31] found a relation with male gender, SBP, DBP, HDL cholesterol and BMI, but not with a family history of early onset cardiovascular disease, smoking or a sedentary lifestyle.

In the present study, the groups with and without microalbuminuria were similar, only presenting a statistically significant difference for HDL cholesterol levels, and the microalbuminuria patients presented values below 40 mg/dl more often.

There is also a great deal of variation in regard to the prevalence of microalbuminuria. In the untreated hypertensive population, the prevalence is considered to be between 20% and 30%, and in the treated hypertensive population it is as high as 25%[22,23], even though some authors accept values between 7% and 40%[15,25]. Explanations for this variation could be different urinary albumin measurement methods, urinary collection errors (when conducted over a period of time) or study group variations in relation to age, ethnic groups or comorbidities[18].

In cross-sectional studies, Jensen et al[32] found a prevalence of 4.7% in hypertensive patients undergoing treatment, whereas Palatini et al[29], Pontremoli et al[31] and Leoncini et al[30] found, respectively, 6.1%, 6.7% and 9% in untreated hypertensive patients.

Table 3 - Relationship between microalbuminuria and target organ lesions in hypertensive patients undergoing treatment

	Group NA (n = 132)	Group MA (n = 21)	Total (n = 153)	p*
TOL present (%)	58 (43.9)	16 (76.2)	74 (48.4)	0.006
Cardiac (%)	49 (37.1)	15 (71.4)	64 (41.8)	0.003
ES/TIA (%)	9 (6.8)	1 (4.8)	10 (6.5)	1.00
PAD (%)	8 (6.1)	2 (9.5)	10 (6.5)	0.62
Retinopathy (%)	2 (1.5)	0	2 (1.3)	0.81

NA – normoalbuminuria; MA – microalbuminuria; TOL – target organ lesion; Cardiac – left ventricular hypertrophy, angina and/or acute myocardial infarction, congestive heart failure; ES – encephalitic stroke; TIA – transient ischemic attack; PAD – peripheral arterial disease.
**: analysis using the chi-square test*

Table 4 – Relationship between microalbuminuria and age group in hypertensive patients undergoing treatment

	Geriatrics (n = 78)	Non-geriatrics (n = 75)	Total (n = 153)	p*
Group NA (%)	66 (84.6)	66 (88.0)	132 (86.3)	0.54
Group MA (%)	12 (15.4)	9 (12.0)	21 (13.7)	

*NA – normoalbuminúria; MA – microalbuminúria; *: teste de qui-quadrado.*

Table 5 – Relationship between microalbuminuria, cardiac lesions and age group in hypertensive patients undergoing treatment

	Geriatrics *		Non-geriatrics	
	Group NA	Group MA	Group NA	Group MA
Cardiac lesion +	27 (40.9)	10 (83.3)	22 (33.3)	5 (55.6)
Cardiac lesion -	39 (59.1)	2 (16.7)	44 (66.7)	4 (44.4)

*NA – normoalbuminuria; MA – microalbuminuria; Cardiac lesion – left ventricular hypertrophy, angina and/or acute myocardial infarction, congestive heart failure; *: $\chi^2 = 7.33$; $p = 0.006$.; The numbers in the brackets indicate the percentages.*

Table 6 – Logistic regression analysis between microalbuminuria, age and cardiac lesions in hypertensive patients undergoing treatment

	Coefficient	Standard Error	Wald	p	OR	95% CI minimum	95% CI maximum
Age ≥ 60 years	0.412	0.347	1.412	0.235	1.510	0.806	3.056
Microalbuminuria	1.481	0.529	7.851	0.005	4.398	1.511	11.519
Constant	-0.672	0.299	5.055	0.025	0.511		

OR – odds ratio; CI confidence interval.

On the other hand, Agewall et al[7] observed microalbuminuria in 25% of their patients receiving antihypertensive treatment, and Agrawal et al[8] found a prevalence close to 30%, in a study involving treated and untreated hypertensive patients. In a prospective study, Redon et al[28] followed a group of hypertensive patients for roughly 2.7 years and observed the progression to microalbuminuria in 11.7% (22/187).

In our study, the microalbuminuria prevalence was 13.7%, a result within the expected range for the type of population studied.

Various studies have demonstrated a positive and independent association between microalbuminuria and cardiovascular disease in both hypertensive patients[7,8] and the general population[12,13].

In 1997, Jensen et al[32] published a study demonstrating that urinary albumin excretion (and not the presence of microalbuminuria) was related to cardiovascular disease, and that the highest blood pressure levels were found in the patients with the highest urinary albumin excretion. In 2000, the same authors[9] published a study that followed hypertensive patients for 10 years and observed the development of ischemic coronary disease in 28% of the patients that had microalbuminuria at the start of the study, whereas this rate was only 8% in the patients with normoalbuminuria.

In the present study, a statistically significant association was found between target organ lesions and microalbuminuria (p=0.006); these lesions were found in approximately ¾ of the patients in this group (76.2% *versus* 43.9% in the normoalbuminuria group). Cardiac lesions had the highest prevalence and maintained a significant association with microalbuminuria (p=0.003), with a frequency of 71.4% of the patients in this group.

Nakamura et al[10] followed hypertensive patients over the age of 65 for eight years, comprising 111 normoalbuminuria patients and 33 microalbuminuria patients. The incidence of cardiovascular disease in the microalbuminuria group was higher (18% *versus* 7%) and the urinary albumin excretion values were related to the incidence of cardiovascular disease.

In the group of geriatric microalbuminuria patients, the majority (83.3%) presented some type of cardiac lesion. In the individuals under age 60, bivariate analysis did not reveal an association between microalbuminuria and cardiac lesions, but the logistic regression analysis demonstrated that microalbuminuria and not age group, was the variable that determined the presence of cardiac lesions.

Since this was a cross-sectional study, we could not establish a causal relationship between microalbuminuria and target organ lesions or, more specifically, cardiac lesions; however we can assume that there is an association between these two conditions, which has also been indicated by the various studies on the subject.

The sample is another point to be considered. Since the population was selected on a convenience basis, the results cannot be extrapolated for the general population; however it can be determined that the results are in agreement with medical literature in the area.

The results of the present study summarize the findings in other studies, and could encourage the development of new studies to further our comprehension on the association between microalbuminuria and systemic hypertension.

Microalbuminuria is an important auxiliary tool in the assessment of hypertensive patients, and should be studied and investigated more thoroughly in medical practice. Microalbuminuria isn't the cause of cardiovascular disease, but its presence helps to identify individuals at high risk to develop it, indicating that they should be followed more closely and receive aggressive treatment for other concomitant risk factors[25].

Conclusion

For the hypertensive population treated at the Internal Medicine Outpatient Healthcare Center and the Cardiology Outpatient Clinic at a University Hospital in the Southern Region of Brazil between April and August 2006, in regard to the proposed objectives, we can conclude:

1. The prevalence of microalbuminuria is 13.7% and that of target organ lesions is 48.4%;

2. There is a statistically significant association between microalbuminuria and target organ lesions. This association holds true in relation to cardiac lesions for the entire study population, including the geriatric group.

Potential Conflict of Interest

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

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Study Association

This study is not associated with any graduation program.

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