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Hypertensive patients with and without kidney disease: assessment of risk factors*

Hipertensos com e sem doença renal: avaliação de fatores de risco

Hipertensivos con y sin enfermedad renal: evaluación de factores de riesgo

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ABSTRACT

Objective: To compare hypertensive patients with and without chronic kidney disease and identify factors associated with their clinical condition and antihypertensive treatment. **Method:** This was a cross-sectional study conducted with patients hospitalized in a general medical ward at a university hospital in the city of São Paulo, Brazil. Data were collected from medical records. Significance was set at $p<0.05$. **Results:** Of the 386 patients studied, 59.3% presented hypertension and, of these, 37.5% presented chronic kidney disease. The data showed an independent association between chronic kidney disease and prior history of diabetes (OR 1.86; CI 1.02-3.41), congestive heart failure (OR 3.42; CI 1.36-9.03) and living with a partner (OR 1.99; CI 1.09-3.69). Regarding antihypertensive treatment, there was a difference ($p<0.05$) between hypertensive patients with and without chronic kidney disease in terms of administering healthcare treatment (93.2% *versus* 77.7%); ongoing use of antihypertensive drugs, (79.1% *versus* 66.4%); higher number of antihypertensive drugs; the use of beta-adrenergic blockers (34.9% *versus* 19.6%), calcium channel blockers (29.1% *versus* 11.2%), loop diuretics (30.2% *versus* 10.5%) and vasodilators (9.3% *versus* 2.1%). **Conclusion:** The hypertensive patients with chronic kidney disease presented a more compromised clinical profile; however, the attitudes of these patients toward antihypertensive treatment were more positive than those without chronic kidney disease.

DESCRIPTORS

Hypertension; Renal Insufficiency, Chronic; Risk Factors; Medication Adherence.

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INTRODUCTION

The concept of patient safety in clinical practice is understood as a fundamental principle in preventing hazards involving patients. According to the World Health Organization[1], patient safety is "the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum." In this sense, managing the risks associated with a disease will directly influence the outcome of a recommended treatment. The present study was based on the consideration of hypertension as an important risk factor for chronic kidney disease, hypertension is among the main risk factors related to this disease.

Chronic kidney disease is a significant global public health problem, with an estimated prevalence between 1.5% and 43.3%[2-3]. Moreover its presence has been associated with greater cardiovascular morbidity and mortality[4-5]. The main risk factors attributed to chronic kidney disease are: increased life expectancy, diabetes mellitus and hypertension[6]. These factors are intimately associated with the socioeconomic development of a given population: On the one hand, improved living conditions and access to healthcare services reduces the number of deaths due to infections and external causes; on the other, higher quality of life can sometimes lead to a sedentary lifestyle and poorer nutritional habits.

The association between hypertension and chronic kidney disease is well known, considering that chronic kidney disease is the greatest cause of secondary hypertension. Hypertension can also determine the emergence of chronic kidney disease and contribute to its progression to the terminal stage. Associations between blood pressure blood pressure levels and kidney function deterioration have been shown by many research studies[7-8].

While diabetes mellitus represents the leading isolated cause of end stage kidney disease in several countries, hypertension is the most common etiology in Brazil, identified among 34% of dialysis patients[8]. Considering that the great relevance of diabetes mellitus in developed countries has been attributed to reduced mortality related with hypertension and other cardiovascular causes, we can argue that greater attention must be given to the health care delivered to hypertensive patients, in order to minimize the risks and profile of morbimortality among them.

In light of this, the hypothesis adopted in the present study was that chronic kidney disease in the hypertensive population would be associated with other risk factors, such as cardiovascular and renal ones. The objectives of this study were to compare hypertensive patients with and without kidney disease and identify factors associated with this clinical condition. The study also analyzed antihypertensive treatment among hospitalized patients in a general medical ward of a university hospital in the city of São Paulo, Brazil.

METHOD

This was a cross-sectional, exploratory and quantitative study conducted between December 2010 and June 2013. It was approved by a research ethics committee (no. 1103/11).

Sample size was calculated for an estimated prevalence of kidney disease of 13%, variation of 5%, type I error of 5% and power of 80%. Under these parameters, sample size was estimated at 386 individuals. Inclusion criteria were being 18 years or older and having been hospitalized in the general medical ward of a university hospital in 2009, in the city of São Paulo, Brazil. We excluded expecting mothers, patients that had been hospitalized for less than 24 hours, absence of serum creatinine in at least two instances during the hospitalization period, and patients who evolved to acute kidney injury during their hospital stay according to Acute Kidney Injury Network[9] criteria (an increase in serum creatinine levels equal or greater than 0.3 mg/dL in patients without a medical diagnosis of chronic kidney disease or a medical diagnosis of acute kidney injury.

Data were collected retrospectively from patient charts and recorded on an instrument created for this purpose. We gathered sociodemographic information (age, gender, marital status, occupation, weight and height); patient medical history, including comorbidities; lifestyle habits such as smoking; healthcare treatment received prior to hospitalization; and ongoing medication use. For the purposes of this analysis, we selected patients who presented a personal medical history or medical diagnosis of hypertension (n=229). Chronic kidney disease was defined as the presence of a medical diagnosis recorded at least on one occasion on the patient chart. To assess blood pressure, we considered the first record in the chart, performed in the morning of each day of the hospitalization period. Controlled hypertension was evaluated according to criteria set forth by the VI Brazilian Guidelines on Hypertension[10], with values lower than 140 mmHg for systolic blood pressure and 90 mmHg for diastolic blood pressure.

Statistical Analysis

Associations between the classification variables and the groups with and without chronic kidney disease were assessed using chi-square tests, the likelihood ratio test, and Fisher's exact test. Regarding the quantitative variables, Student's t-test was used to compare the means of normally distributed variables. The biosocial and comorbidity variables with a statistical significance lower than 0.2 according to univariate analysis were used in the correction of the multiple logistic regression model, in addition to age in years (continuous variable) and history of diabetes. P-values less than 0.05 (bilateral) were considered statistically significant.

RESULTS

Of the 386 patients assessed, more than half (59.3%) presented hypertension. The data in Table 1 demonstrate that hypertensive patients with and without chronic kidney disease presented similarities regarding: slight predomi-

Table 1 - Biosocial characteristics of hypertensive patients hospitalized in a general medical ward, with and without chronic kidney disease - São Paulo, Brazil, 2014.

Variables	With chronic kidney disease (N=86)		Without chronic kidney disease (N=143)		Total (N=229)		p-value
	N	%	N	%	N	%	
Gender							0.365
Male	45	52.3	66	46.2	111	48.5	
Female	41	47.7	77	53.8	118	51.5	
Ethnicity							0.397
White	53	61.6	96	67.1	149	65.1	
Non-white	33	38.4	47	32.9	80	34.9	
Marital status (N=226)							**0.047**
Single	30	35.7	70	49.3	100	44.2	
With a partner	54	64.3	72	50.7	126	55.8	
Occupation (N=220)							0.862
Active worker	31	38.3	59	42.4	90	40.9	
Retired	26	32.1	39	28.1	65	29.5	
Homemaker	21	25.9	34	24.5	55	25.0	
Others*	3	3.7	7	5.0	10	4.5	
Age (years. mean±sd)	65.6±14.3		64.8±14.5		65.1±14.4		0.678
Body mass index (kg/m²) (N=79)							0.876
Median (1°.-3°. quartiles)	27.4 (23.3-30.9)		26.4 (24.0-29.8)		26.8 (23.9-29.9)		

* Unemployed (6); Student (4).

nance of female patients (51.5%); white ethnicity (65.1%); active workers (40.9%). Body mass index was compatible with overweight [26.8 (23.9–29.9) kg/m^2]; and the most predominant age group in both test groups consisted of patients in their sixties [65.1 (14.4 years)]. The hypertensive patients with chronic kidney disease were different, compared to those without chronic kidney disease because they lived with a partner (64.3% *versus* 50.7%, p=0.047).

Almost all of the hypertensive patients with and without chronic kidney disease (95.3% and 92.3%, respectively) had at least one comorbidity recorded at the time of hospital admission. The data presented in Figure 1 show a significant difference (p<0.05) between patients with and without chronic kidney disease regarding history of diabetes (53.5% *versus* 36.4%) and congestive heart failure (19.8% *versus* 7.0%). There was no difference between groups in terms of smoking history, however, considering the current smoking status of hypertensive patients (smokes, stopped, never smoked), there was a significant difference, with a lower percentage of smokers in the chronic kidney disease group (9.9% *versus* 25.0%, p=0.022).

Multiple logistic regression analysis (Table 2) demonstrated that history of diabetes and congestive heart failure were independently associated with chronic kidney disease. The risk of presenting these comorbidities was approximately two and three times greater, respectively. Living with a partner also was associated with the presence of chronic kidney disease even after correction for other variables, reflecting a two-fold risk. Current or prior smoking was at the threshold of significance (OR 0.54, 95% CI 0.29-1.00).

Regarding hypertension treatment prior to hospitalization (Table 3), most patients had been undergoing treatment, with emphasis on the chronic kidney disease group (93.2% *versus* 77.7%, p=0.005). Almost a third of the

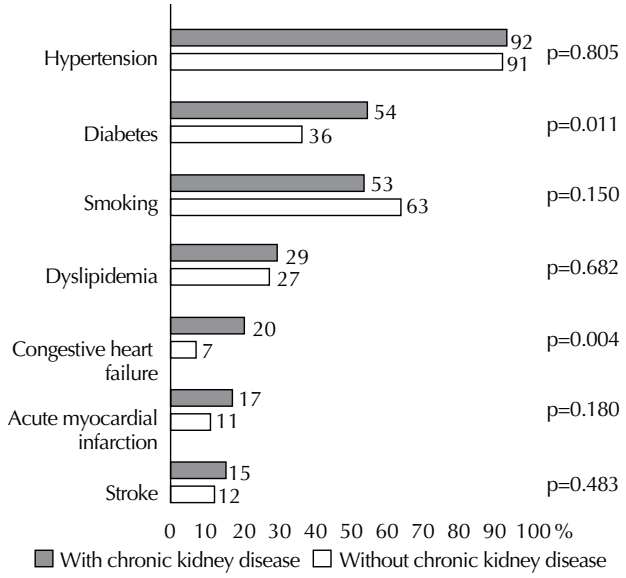


Figure 1 - Comorbidities and smoking among hypertensive patients with and without chronic kidney disease hospitalized in a general medical ward, - São Paulo, Brazil, 2014.

Table 2 - Predictors of chronic kidney disease among hypertensive patients at a general medical ward according to multivariate analysis - São Paulo, Brazil, 2014.

Variables	Odds ratio	95% Confidence interval		P-value
Age (by additional year)	0.99	0.97	1.02	0.579
Marital status (with partner)	1.99	1.09	3.69	**0.026**
Smoking	0.54	0.29	1.00	**0.050**
Diabetes mellitus	1.86	1.02	3.41	**0.042**
Congestive heart failure	3.42	1.36	9.03	**0.010**
Acute myocardial infarction	1.66	0.66	3.97	0.281

Table 3 - Treatment at healthcare services and continuous use of antihypertensive drugs by hypertensive patients hospitalized in a general medical ward, with and without chronic kidney disease - São Paulo, Brazil, 2014.

Variables	With Chronic Kidney Disease (N=86)		Without Chronic Kidney Disease (N=143)		Total (N=229)		p-value
	N	%	N	%	N	%	
Treatment at healthcare service (N=194)							**0.005**
Yes	68	93.2	94	77.7	162	83.5	
No	5	6.8	27	22.3	32	16.5	
Number of antihypertensive drugs							**0.001**
None	18	20.9	48	33.6	66	28.8	
One	13	15.1	40	28.0	53	23.1	
Two to three	40	46.5	45	31.5	85	37.1	
More than three	15	17.4	10	7.0	25	10.9	
Angiotensin-converting enzyme inhibitors							0.849
Yes	39	45.3	63	44.1	102	44.5	
No	47	54.7	80	55.9	127	55.5	
Beta-adrenergic blockers							**0.010**
Yes	30	34.9	28	19.6	58	25.3	
No	56	65.1	115	80.4	171	74.7	
Thiazide diuretics							0.328
Yes	13	15.1	29	20.3	42	18.3	
No	73	84.9	114	79.7	187	81.7	
Calcium channel blockers							**0.001**
Yes	25	29.1	16	11.2	41	17.9	
No	61	70.9	127	88.8	188	82.1	
Loop diuretics							**<0.001**
Yes	26	30.2	15	10.5	41	17.9	
No	60	69.8	128	89.5	188	82.1	
Potassium sparing diuretics							0.134
Yes	7	8.1	5	3.5	12	5.2	
No	79	91.9	138	96.5	217	94.8	
Angiotensin II receptor blockers							0.764
Yes	5	5.8	7	4.9	12	5.2	
No	81	94.2	136	95.1	217	94.8	
Direct vasodilators							**0.015**
Yes	8	9.3	3	2.1	11	4.8	
No	78	90.7	140	97.9	218	95.9	
Alpha-adrenergic blockers							0.530
Yes	3	3.5	3	2.1	6	2.6	
No	83	96.5	140	97.9	223	97.4	

hypertensive patients (28.8%) did not take antihypertensive medication continuously, however, among those that did, the percentage was higher among those with chronic kidney disease when compared to those without chronic kidney disease (79.1% *versus* 66.4%, p=0.041). Hypertensive patients with chronic kidney disease also took a greater number of antihypertensive drugs (p=0.001) than those without chronic kidney disease.

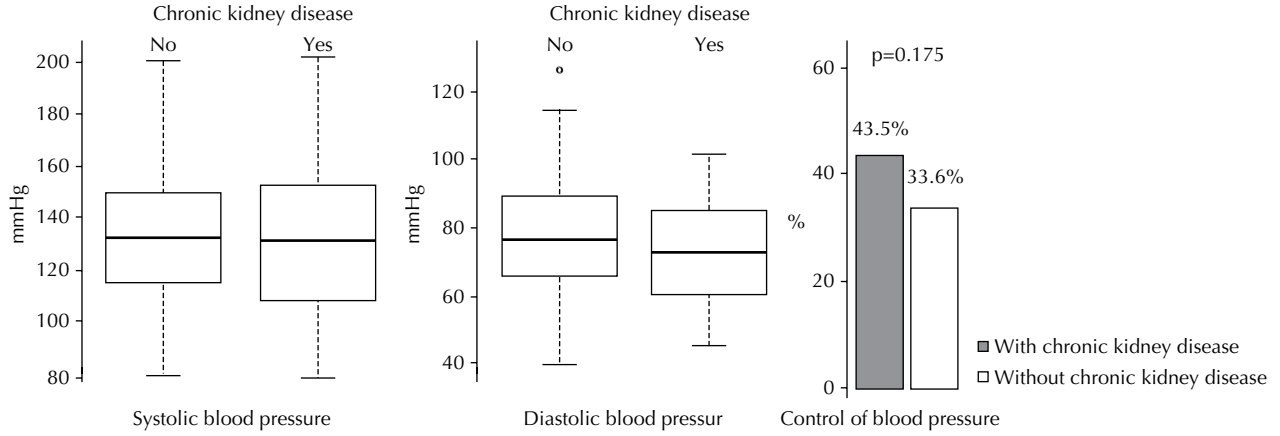
The most commonly used class of antihypertensive drugs was angiotensin-converting enzyme inhibitors (44.5%) and beta-adrenergic blockers (25.3%). There was a significant difference (p<0.05) between hypertensive patients with and without chronic kidney disease regarding the use of beta-adrenergic blockers (34.9% *versus* 19.6%), calcium channel blockers (29.1% *versus* 11.2%), loop diuretics (30.2% *versus* 10.5%) and direct vasodilators (9.3% *versus* 2.1%).

Blood pressure on the first day of hospitalization was recorded for 191of the patients in the sample (52.8%). Mean systolic blood pressure of the study population was 135.6 mmHg and no differences were found between patients with and without chronic kidney disease. In turn, diastolic blood pressure was lower among hypertensive patients with chronic kidney disease (75.6 *versus* 80.6 mmHg, p=0.030). No significant difference was found between groups regarding the frequency of blood pressure control (Figure 2).

DISCUSSION

In this study, hypertensive patients with chronic kidney disease chronic kidney disease stood out in comparison with those without chronic kidney disease in terms of presenting higher rates of diabetes mellitus and congestive heart failure. In fact, both comorbidities have been shown to contribute to the onset of chronic kidney disease.

Oxidative stress produced by hyperglycemia and proteinuria, hyperperfusion and kidney hyperfiltration, are factors involved in the pathogenesis of chronic kidney disease. Factors commonly associated with diabetes, such as obesity and cardiovascular diseases, contribute equally to the development of kidney failure[11]. End stage kidney



CKD=Chronic Kidney Disease

Figure 2 - Blood pressure on the first day of hospitalization and control among hypertensive patients hospitalized in a general medical ward, with and without chronic kidney disease - São Paulo, Brazil, 2014.

disease in patients with diabetes mellitus type 2, supposedly associated with diabetic glomerulosclerosis, has taken on great importance over the last few decades in countries with Western lifestyles. Its incidence increased dramatically in the 1980s and 1990s, going from 23.4 pmp (in 1984) to 66 pmp (in 1994) in Japan, and from 29.2 pmp to 107 pmp in the United States in the same period[12]. Even though the United States presented a 3.9% per year reduction in the incidence of end stage kidney disease adjusted for age from 1996 to 2006, diabetes is still the leading cause of kidney failure in the country (44% of new cases treated)[13], similar to Mexico, Malaysia, Taiwan, New Zealand, Japan, Israel, and other countries [14]. Diabetes mellitus ranks as the second baseline diagnosis for patients undergoing kidney replacement therapy (dialysis) in Brazil, with a frequency of 29% in 2012[15].

Studies have suggested that congestive heart failure can be an important cause of progressive kidney failure, as approximately 50% of individuals with this disorder have chronic kidney disease[16]. In contrast, a study with a sample taken from the NHANES III found that the prevalence of congestive heart failure among patients with chronic kidney disease with and without diabetes, respectively, was 39.9% and 54.1%, significantly ($p<0.05$) lower than those of patients without these diseases[17]. Even though decreased cardiac debt related to the cardiomyopathy itself or its treatment can contribute to the genesis of progressive kidney failure, the main etiologies of congestive heart failure are hypertensive and ischemic, both closely linked to hypertension[6].

The study emphasized that the co-existence of hypertension with other factors associated with kidney damage can be very harmful to these patients' prognosis, especially when uncontrolled. A study with hypertensive patients with diabetic nephropathy whose mean duration of follow-up was 3.4 years, identified a hazard ratio for the progression of chronic kidney disease, kidney failure, or death as being 66% greater ($p<0.001$) among individuals whose systolic blood pressure was equal or greater to 140 mmHg, than those with lower systolic blood pressure levels[18].

Regarding lifestyle habits, there was a higher percentage of smokers in the group without chronic kidney disease, which was significant ($p<0.05$) for currently active smokers and was almost significant with regards to those who were former smokers. This finding differs from those of several other studies that have shown an association between smoking and the development and progression of chronic kidney disease[19-21]. However, the retrospective nature of the present study and the data gathered from patient charts did not allow for the assessment of data relevant to this habit such as time of abstinence among those who reported being former smokers. Many smokers tend to stop smoking when they reach the more severe phases of the disease, which contributes to a lower percentage of smokers found in cross-sectional studies with chronic kidney disease patients. Furthermore, this observation may be a product of a selection bias inherent to cross-sectional studies: patients with chronic kidney disease and smokers may be underrepresented in the sample due to higher mortality rates.

The association between chronic kidney disease and marital status was also significant ($p<0.05$), with a predominance of individuals living with partners. Living with a partner has been considered an indication of family support, which would be related to better treatment adherence by patients with chronic diseases and better health outcomes [22-23]. This positive effect of living with a partner was not observed in the present study. Factors such as time spent and quality of the couple's relationship, in addition to other social support networks may be involved in better levels of chronic disease treatment management and prevention of renal complications.

The present study also found that the rate of controlled blood pressure among patients with and without chronic kidney disease on the first day of their hospital stay was approximately 40%, a percentage that falls within the range of blood pressure control described in Brazil. In recent years, population-based studies in Brazil have shown blood pressure control rates ranging between 30% and 50%[24]. However, the control of blood pressure can be more compromised

in the presence of comorbidities and end organ damage. A study conducted with hypertensive patients with end organ damage receiving ambulatory treatment showed that less than a third of individuals presented controlled blood pressure[22]. In another study, blood pressure control was assessed according to specific targets by stratifying cardiovascular risk and only 32.4% of hypertensive patients with nephropathies and proteinuria greater than 1 g/L were controlled, compare with 61.7% of stage I and II hypertensive patients with low or moderate cardiovascular risk[25].

Despite the existence of proven effective measures to reduce cardiovascular morbimortality due to raised blood pressure levels, control of this disease is still low. This fact has been attributed to low adherence to antihypertensive treatment. Treatment adherence among these patients represents a real challenge, as it is a result of the interaction of several individual, structural and disease- and treatment-related characteristics. Adherence refers to the behavior of individuals and compliance with a recommended health treatment. Missing appointments and interrupting drug therapy are aspects that have been commonly used to assess treatment adherence among hypertensive patients[26-27].

A significant portion of the hypertensive patients in the present study presented behavior that could reflect lack of antihypertensive treatment adherence, such as not taking antihypertensive drugs continuously, even with a prior diagnosis of hypertension or comorbidities compatible with end organ damage. The rate of nonadherence to drug therapy (28.8%) was higher than that observed in a representative sample of the Brazilian population in 2008 (17%)[28]. Nonadherence to antihypertensive treatment can contribute to the hospitalization of the studied patients, considering that cardiovascular morbidity was significant both in hypertensive patients with and without chronic kidney disease. Most hypertensive patients (67.2%) presented some comorbidity in addition to hypertension and chronic kidney disease recorded on their charts.

CONCLUSION

Hypertension in chronic kidney disease was associated with other risk factors for the development and progression of renal failure in hypertensive patients admitted to a general medical ward in a university hospital in the city of São Paulo, Brazil. More than half of the hypertensive patients presented uncontrolled hypertension and almost a third presented characteristics compatible with nonadherence. The results point to the need for more wide-reaching actions regarding healthcare of hypertensive patients in Brazil. Safety measures, which assess the characteristics of patients and their outcome, in addition to the control of associated risk, via health education actions, encouraging decision-making and self-care are essential to treatment adherence and to preventing complications and hospital morbidity.

In light of the increasing impact of noncommunicable chronic diseases in Brazil, several public health policies have been adopted to prevent and control these conditions. Such policies range from regulating tobacco use in public environments to offering free drug therapy to prevent cardiovascular events in high-risk patients. Even though standard cardiovascular mortality rates by age have decreased over the last few decades, they are still much higher than those observed in other countries. Cardiovascular causes represent the leading cause of death among Brazilians and high morbimortality rates in the country has been attributed especially to hypertension. Moreover, hypertension constitutes the main cause of kidney failure treated with dialysis in Brazil. For this reason, healthcare professionals, especially nurses, must prioritize care offered to hypertensive individuals, through actions such as hypertension surveillance, comprehensive care and health promotion. Regarding chronic kidney disease, treating hypertension and diabetes mellitus can also be effective in its treatment.

In the context of healthcare delivered to hypertensive patients, the goal of the treatment is to control the disease. The absence of or inadequate control contribute to complications involving end organ damage, such as kidney disease, and can even lead to the need for hospitalization. Therefore, comprehensive care in primary healthcare services, where most hypertensive patients are cared for, together with the support of specialized institutions, compose a structure of commitment and availability that ensures safe and effective care. The fragmentation of health care is not safe for patients. With the goal of caring for patients in their totality and individuality, nursing professionals must promote actions that meet the real needs of hypertensive patients.

RESUMO

Objetivo: Comparar pacientes hipertensos com e sem doença renal e identificar fatores associados à condição clínica e tratamento anti-hipertensivo. **Método:** Estudo transversal realizado com pacientes admitidos em clínica médica de um hospital universitário da cidade de São Paulo. Os dados foram coletados por meio de análise do prontuário. Valores de p<0,05 foram considerados significantes. **Resultados:** Dos 386 pacientes avaliados, 59,3% eram hipertensos e destes 37,5% tinham doença renal crônica. Houve associação independente da presença de doença renal crônica para antecedentes de diabetes (OR 1,86; IC 1,02-3,41) e de insuficiência cardíaca congestiva (OR 3,42; IC 1,36-9,03); além do fato de viver com companheiro (OR 1,99; IC 1,09-3,69). Quanto ao tratamento anti-hipertensivo, houve diferença (p<0,05) entre os hipertensos com e sem doença renal em relação a fazer acompanhamento de saúde (93,2% *vs* 77,7%); uso contínuo de medicamentos anti-hipertensivos, (79,1% *vs* 66,4%); maior número de medicamentos anti-hipertensivos; uso de bloqueadores beta-adrenérgicos (34,9% *vs* 19,6%), bloqueadores dos canais de cálcio (29,1% *vs* 11,2%), diuréticos de alça (30,2% *vs* 10,5%) e vasodilatadores (9,3% *vs* 2,1%). **Conclusão:** Os hipertensos com doença renal crônica apresentaram perfil clínico mais comprometido, porém em relação ao tratamento anti-hipertensivo as atitudes foram mais positivas do que os sem doença renal.

DESCRITORES
Hipertensão; Insuficiência Renal Crônica; Fatores de Risco; Adesão à Medicação.

RESUMEN
Objetivo: Comparar pacientes hipertensivos con y sin enfermedad renal e identificar factores asociados relacionados a la condición clínica y tratamiento anti-hipertensivo. **Método:** Estudio trasversal con pacientes en clínica médica de un hospital universitario de São Paulo. Los datos fueron recolectados mediante análisis de archivo. Valores de p<0,05 fueron considerados significantes. **Resultados:** De los 386 pacientes evaluados, 59,3% era hipertensivo y, entre estos, 37,5% sufría de enfermedad renal crónica. Fue encontrada asociación independiente de la presencia de enfermedad renal crónica para antecedentes de diabetes (OR 1,86; IC 1,02-3,41) y de insuficiencia cardíaca congestiva (OR 3,42; IC 1,36-9,03); además del hecho de vivir con pareja (OR 1,99; IC 1,09-3,69). Respecto al tratamiento anti-hipertensivo, fue encontrada diferencia (p<0,05) entre los hipertensivos con y sin enfermedad renal respecto a hacer monitoreo de salud (93,2% *vs* 77,7%); uso continuo de medicamentos anti-hipertensivos, (79,1% *vs* 66,4%); mayor número de medicamentos anti-hipertensivos; uso de bloqueadores beta-adrenérgicos (34,9% *vs* 19,6%), bloqueadores de los canales de calcio (29,1% *vs* 11,2%), diuréticos de asa (30,2% *vs* 10,5%) y vasodilatadores (9,3% *vs* 2,1%). **Conclusión:** Los hipertensivos con enfermedad renal crónica mostraron perfil clínico más comprometido pero, respecto al tratamiento anti-hipertensivo, las actitudes fueron más positivas que entre aquellos sin enfermedad renal.

DESCRIPTORES
Hipertensión; Insuficiencia Renal Crónica; Factores de Riesgo; Cumplimiento de la Medicación.

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