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Predictors of Kidney Damage in Newly-Diagnosed Hypertensive Nigerians

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ABSTRACT

Systemic hypertension is an important cause of chronic kidney disease. Identifying predictors of hypertensive kidney damage provides clinicians with opportunity for appropriate therapeutic interventions. This will forestall kidney damage and prevent development of chronic kidney disease. The study aims at determining predictors of kidney damage using microscopic haematuria as surrogate marker in newly diagnosed hypertensive patients. A cross sectional study of 138 newly diagnosed hypertensive Nigerian, matched with age and sex controls was conducted. The surrogate marker of kidney damage was microscopic haematuria defined as ≥ 3/hpf, determined by examination of urine sediment under a bright field microscope after application of Sternheimer's stain. Potential predictors of kidney damage evaluated were: age, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), pulse pressure (PP), and body mass index (BMI). Mean age of the patients was 43.2±9.6years and 76 (55%) were males. SBP correlates positively with kidney damage (r=0.209, p=0.048). Stepwise regression models identified SBP as the best sole predictor of kidney damage (r=0.557, r^2=0.310, adjusted r^2=0.272, df=1, P=0.011), followed by age (r=0.72, r^2=0.505, adjusted r^2=0.447, df=2, P=0.019). Other variables were rejected by the model (probability level of entrance was ≤ 0.05 and removal, 0 ≥ 0.1). The study suggests that systolic blood pressure may predict kidney damage in newly diagnosed hypertensive patients, and it seems to be amplified with increasing age. A longitudinal study with larger population is recommended to confirm this relationship.

Keywords: *Predictors, kidney damage, microscopic haematuria, hypertension, Nigerians*

Conflict of interest: None

INTRODUCTION

Systemic hypertension is a major public health problem and is predicted to remain same in the next decade [1]. It is a well recognized renal and cardiovascular risk, and a leading cause of chronic kidney disease (CKD) [1]. It is also a potent predictor of progression of CKD which has recently attracted attention of the global nephrology community because of its growing incidence and prevalence [2]. The associated morbidities and mortalities and enormous healthcare costs of managing CKD, particularly of the end-stage kidney disease (ESKD) are major concerns. It is for these reasons that preventive measures are widely and vigorously advocated as the most effective strategy to reduce CKD burden. Clinical and epidemiological data have shown that blacks have enhanced susceptibility to developing hypertensive kidney damage. A contributory factor is their propensity for developing intrinsic renal vascular injury facilitated by unique clinical characteristics some of which are largely modifiable or amenable to therapeutic interventions [3].

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Therefore, identifying factors that determine or promote kidney injury early in hypertensive patients would provide opportunity for targeted therapy to prevent initial and further kidney damage thereby reducing the incidence, prevalence and overall impact of CKD/ESKD. One of the veritable tools for early detection of kidney diseases is urine analysis which incorporates microscopy with dipstick tests [4].

The guidelines for the management of hypertension produced by both World Health Organization/ International Society of Hypertension (WHO/ISH) in 1999 and International Forum for Hypertension control and prevention in Africa (IFHA) recommended examination of urinary sediment as a complement to dipstick test in the evaluation of hypertensive patients[5,6]. While dipstick tests are commonly and routinely utilized in hypertensive patients, their urine is rarely examined for .sediments. Indeed literature is extremely sparse on the subject of urinary sediment and hypertension. Microscopic examination of urine is a simple, cheap and cost-effective method of detecting sub-clinical kidney damage. These make it relevant for economically disadvantaged populations who cannot afford the cost of novel markers of kidney damage for majority of their patients. Abnormal urinary sediment manifesting as microscopic haematuria with characteristic dysmorphic features is an evidence of glomerular bleeding in response to varieties of insults[7]. These insults may be initiated by an immunologically mediated disease such as glomerulonephritis or haemodynamically mediated as in systemic hypertension .

Systemic hypertension causes kidney damage predominantly by transmission of the arterial pressure to the glomerular capillaries which overwhelm the intrinsic renal autoregulatory process leading to glomerular bleeding from capillary injury. Haematuria of glomerular origin, like proteinuria, decreased glomerular filtration rate (GFR) or elevated levels of serum urea and creatinine is a marker of kidney damage. There are few studies among Nigerian hypertensive population that assessed factors associated with kidney damage. One of such studies was carried out on treated hypertensive patients [8]. We are not aware of any study that reported predictors of kidney damage using abnormal urinary sediment as the marker in newly diagnosed hypertensive Nigerians, hence this study. The outcome may help to identify target (s) for more aggressive and focused therapy that will protect the kidney from effects of hypertension.

MATERIALS AND METHODS

This is a cross sectional study of one hundred and thirty-eight newly diagnosed adult Nigerian hypertensive patients, who were compared with the same number of age and sex matched apparently healthy non-hypertensive controls from the general population. Ethical clearance was obtained from the ethical and research committee of university of Ilorin Teaching Hospital. Subjects with other conditions associated with urinary sediment formation including urinary tract infection were excluded. The subjects' clinical and biographic data were collated in the outpatient clinic of the hospital while the laboratory components were carried out at the hospitals' chemical laboratory and renal unit laboratory. The surrogate marker of kidney damage was significant microscopic haematuria defined as ≥3/hpf. This was determined by examination of urine sediment under a bright field microscope having centrifuged the urine and application of supravital Sternheimer's stain. Sternheimer's stain is a mixture of Copper-phthalocyanine dye, national fast blue and a xanthene dye (pyronin B) used as an alternative to phase contrast microscope to enhance identification of elements of urinary sediment. The sediment preparation and staining technique were as follows: 10ml of early morning "first void" clean catch urine was collected in a sterile tube and centrifuged for 5minutes. The supernatant was decanted leaving 0.5ml of the sediment. A drop of Sternheimer's stain was added to the 0.5ml sediment and left for 10

Table 1: Age distribution of the subjects

Age (yrs)	Patients		Controls		P value
	n (%)		n (%)		
20-29	11	8	11	8	1.0000
30-39	37	26.8	33	23.9	0.5800
40-49	58	42	63	45.7	0.5442
50-59	25	18	24	17.4	0.8748
60-69	4	2.9	4	2.9	1.0000
70-79	3	2.2	3	2.2	1.0000
Mean age	43.21 (±9.65)		43.19 (±9.55)		0.9862

Table 2: Urinary sediment cells in patients and controls

Cells	(per hpf)	Patients n (%)	Controls n(%)	P value
RBC	Nil	90 (65.2)	119(86.2)	0.0000
	1-2	27(19.6)	14(10.2)	0.0278
	> 2	21(15.2)	5(3.6)	0.0010
WBC	Nil	128(92.8)	125(90.6)	0.5130
	1-2	10(7.2)	13(9.4)	0.5130
	> 2	-	-	-

RBC, red blood cell; WBC, white blood cell

minutes and then examined under the bright-field microscope. Potential predictors of kidney damage evaluated were: age, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), pulse pressure (PP), and body mass index (BMI). SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) statistical soft ware was used to analyze the data. The strength of association between the variables and kidney damage was determined by correlation statistics while regression methods were used to quantify the association and to predict kidney damage.

RESULTS

There were seventy-six (55%) males in the patients and eighty (58%) in control group. The age distribution is shown in table 1. Sixty percent of the patients were within 40-59years. Significant proportions of the

Table 3: Correlates of microscopic haematuria in hypertensive patients

Parameters	Correlation coefficient (r)	p value
Age (years)	0.121	0.921
Body mass index (kg/m^2)	0.088	0.409
Systolic blood pressure (mmHg)	0.209	0.048
Diastolic blood pressure (mmHg)	0.156	0.143
Mean arterial blood pressure (mmHg)	0.185	0.080
Pulse pressure (mmHg)	0.186	0.080
Urea (mmol/L)	0.049	0.649
Cr(umol/L)	0.165	0.120
Creatinine clearance (ml/min)	-0.175	0.291

Table 4: Predictors of kidney damage in hypertensive patients

Predictors	r	r^2	adjusted r^2	df	P
1st Model					
Systolic blood pressure	0.557	0.312	0.272	1	0.011
2nd Model					
Systolic blood pressure & Age	0.72	0.505	0.447	2	0.019

P of entrance≤ 0.05; removal ≥0.1

patients are young with about a quarter within 30-39years. Table 2 depicts urinary sediment cells, the erythrocytes and leucocytes. There was a significant difference between the prevalence of microscopic haematuria in patients (15%) and the control group (3.6%) (p=0.001). The results of the correlation of kidney damage with the variables are shown in table 3. Only SBP correlated positively (r=0.209) and significantly with kidney damage (p=0.048). The stepwise regression analysis identified SBP as the best independent predictors of kidney damage in the first model (r^2 = 0.312; p=0.011) while SBP and age were identified in the second model (r^2 =0.505; p=0.001, P=0.019) with entrance level at $p \leq 0.05$, and removal at $p \geq 0.1$ (table 4).

DISCUSSION

Systemic hypertension as a major cause of cardiovascular and chronic kidney disease is associated with significant adverse clinical outcomes, especially in resource poor settings of which sub-Saharan African countries are the most affected. Efforts towards reducing the burden of hypertension and its clinical consequences should aim at early identification of risk markers and risk factors that are potential targets for intervention. Sub-clinical kidney damage in form of abnormal urinary sediment (microscopic haematuria) was detected in 15.2% of patients in this study which is significantly higher than 3.6% reported by Ratto *et al* [9] among the Spanish population. This is in support of the fact that blacks have intrinsic susceptibility to hypertensive kidney injury. Studies in black populations have consistently corroborated this observation by showing hypertension to be a major cause of kidney disease. In Nigeria, Ojogwu [10] had shown that hypertension was the cause of ESKD in 43% of 1980 patients studied prospectively. Similarly, Akinsola *et al* [11] reported that hypertension was second to chronic glomerulonephritis as a cause of Kidney failure. Furthermore, among treated hypertensive patients, CKD measured by estimated GFR, abnormal serum chemistry and urine sediment was observed in 18% of patients [8]. In African American population, hypertension remains the leading cause of CKD. Risk factors that enhance development of CKD/ESKD in hypertensive patients include earlier age of onset of hypertension, long standing severe hypertension, family history and black race [12]. Additional factors reported in African Americans are lower socioeconomic status leading to inadequate health care, illicit drug use and utilization of antihypertensive drugs with less reno-protective effect to treat their BP[3]. Genetic and prenatal programming conferring low birth weight and associated reduced nephron number with consequent development of hypertension and kidney disease has been suggested [13]. In African people who are generally associated with poor socioeconomic status, poor health care services and malnutrition, this idea would be most applicable. The age distribution of the patients shows that significant proportion were young with a quarter less than 40years of age. Blacks have generally been shown to develop hypertension and associated target organ damage at relatively younger age compared with their white counterparts [14]. These suggest that hypertension management guidelines in blacks should recognize these risk indicators and prescribe a more aggressive treatment that would help to attenuate both kidney and cardiovascular damage. The hallmark of this study was the observation that systolic blood pressure correlated positively and significantly with kidney damage. This effect seems to be amplified by increasing age. This observation is in support of other studies that had recognized SBP as a more potent risk factor for development of chronic Kidney disease in hypertensive patients. In a 15year follow-up study of American hypertensive men, systolic pressure was clearly shown to be better than diastolic pressure as a predictor of endstage renal disease, and the risk increases with severity of the BP [15]. The finding was later supported by the work of He *et al* [16].

Among treated hypertensive Nigerians, Ayodele *et al* [8] found a significant association between SBP and target organ damage which include CKD but no association between DBP or pulse pressure and target organ damage. In Framingham study in the preceding four decades, Kannel *et al* had demonstrated that SBP confers a risk for coronary heart disease [17]. Ten years later, he also showed similar relationship of SBP with stroke [18]. More evidences have accumulated in recent times in support of SBP (among other BP components) as the most potent predictor of not only kidney damage but also cardiovascular morbidity and mortality. In a study of 4712 French men, Benetos et al had reported an association of SBP with cardiovascular diseases [19]. The multiple risk factor intervention trial (MRFIT) study on the other hand showed that death rate from coronary artery disease was directly related to the level of SBP in 316,099 middle-aged men during

a 12-year follow-up period [20]. In addition; Systolic Hypertension in the Elderly Study (SHES) documented a significant reduction in stroke by treating isolated systolic hypertension [21]. All the foregoing data are in contrast to earlier practice that assumes DBP to be more important than SBP as a cause of target organ damage in hypertensive patients. This may be responsible for the poor control reported in many studies as focus of therapy and measure of treatment efficacy neglected SBP. Our study also demonstrated an amplification of the predictive power of SBP on kidney damage with increasing age. This is not surprising because older age has long been recognized to be associated with both kidney and cardiovascular diseases, and that isolated systolic hypertension is a common occurrence in elderly people. We did not observe an association of MAP, PP and DBP with kidney damage in this study.

The small sample population and cross sectional design of our study may be contributory factors. However, studies have shown that MAP, PP and DBP are also predictors of cardiovascular disease [22]. Sequel to evidences supporting SBP as a more potent cardiovascular and renal risk, it has been recommended for identification as a primary determinant of outcomes and a useful tool for risk stratification when evaluating patients with hypertension or those suffering for hypertension-related clinical events. It is also recommended that SBP should be a focus of more aggressive treatment. Clinicians involved in hypertension management particularly those practicing in the Sub-Saharan region have therefore been advised to change their attitude towards BP management and treat SBP as a more important component while not undermining DBP[23].

CONCLUSION

This study suggests that SBP may be the best predictor of the damage which seems to be amplified by increasing age. However, the small population sample and the cross sectional design of the study preclude a far reaching conclusions. A longitudinal study with large population size is recommended to confirm this relationship.

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