AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 36 NUMBER 2 JUNE 2007

ISSN 1116—4077

Afr. J. Med. Med. Sci. (2007) 36, 95-101

Kidney function and clinical correlates in newly diagnosed hypertensives attending a University Teaching Hospital in Southwest Nigeria

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Summary

Hypertension is associated with development of cardiovascular and kidney complications. Low awareness of hypertension leads to late presentation and development of complications. Studies have also shown that chronic kidney disease is often undiagnosed and patients present late. In view of the aforementioned, the prevalence and clinical correlates of decreased kidney function in newly diagnosed hypertensives were assessed. The study was carried out at LAUTECH Teaching Hospital, Osogbo, Nigeria. One hundred and forty three patients satisfied the inclusion criteria. Hypertension was defined by SBP ≥ 140 and / or DBP ≥ 90 mm Hg. Kidney function was assessed by glomerular filtration rate (GFR) using Modification of Diet in Renal Disease (MDRD) formula. Patients with GFR < 60 mL / min were defined as having decreased kidney function. Determinants of decreased kidney function were assessed. Thirty three patients (23.1 %) have decreased kidney function. On univariate analysis, age, educational status, BMI, SBP and DBP were significantly associated with decreased kidney function. After logistic regression, age and BMI were significantly associated with decreased kidney function. Decreased kidney function was present in 23.1 % of the study population. These patients stand a higher risk of faster progression of kidney disease and cardiovascular complications. This finding underscores the need to improve the awareness of hypertension in the population.

Keywords: *Kidney function, newly diagnosed hypertension, and clinical correlates*

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Introduction

Systemic hypertension is prevalent in Nigeria with reported prevalence rates varying from 9 – 20 % [1-3]. Various population studies have documented low awareness rates of hypertension despite the fact that it is relatively easy to detect and diagnose hypertension [1,4,5]. In Nigeria, the level of awareness of hypertension according to the National Non-communicable Disease Survey was 33.8 % [1]. The import of this low awareness is the development of cardiovascular and kidney complications before presentation in the hospital.

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Hypertension is one of the leading causes of chronic kidney disease (CKD) in Nigeria [6,7]. The development of CKD is associated with a 5 to 10 times higher risk of death form end-stage kidney disease, a higher risk of development of congestive cardiac failure and other cardiovascular events and a 1.8 to 2.9 higher health care cost [8-10]. The earlier the kidney disease is detected, the longer effective therapy can provide dialysis-free survival and associated reduction in dialysis and transplantation expenses and disabilities [11]. Also, various reports have shown that the rate of progression of kidney disease depends partly on the baseline kidney function before initiation of therapy [12]. However, studies have also shown that CKD is often undiagnosed and patients with chronic kidney failure often presents late [13,14]. Late presentation of patients with CKD presents the clinician with lost opportunity to initiate measures to delay or halt the progression of kidney disease; necessitates emergency dialysis with its attendant higher morbidity and mortality; jeopardizes the choice of the mode of dialysis; endangers the ability to maintain prolonged vascular access; precludes prolonged preparation of the patient for care and necessitates prolonged hospitalization with excessive use of health care resources [15].

In view of the foregoing, the kidney function of newly diagnosed patients with hypertension was assessed with a view to determining the prevalence of decreased kidney function in this cohort of patients.

Subjects and methods

The study was carried out at the Medical Outpatient Department (MOP) of Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria between January 2004 and June 2005. Ethical approval for the study was obtained from the institution Ethical Committee.

The study population consisted of 143 consecutive patients who satisfied the inclusion criteria. The inclusion criteria included newly diagnosed hypertensives who have not been on antihypertensives.

The exclusion criteria for the study were:

- patients who had been on antihypertensives;
- those with primary kidney disease as suggested by clinical presentation, presence of active urinary sediments such as red blood cells, cellular cast, granular cast; and utrasonographic findings such as presence of cysts in the kidneys;
- patients with diabetes mellitus to avoid the confounding effects of diabetes mellitus on kidney function. Diabetes mellitus was diagnosed by the presence of fasting plasma glucose ≥ 126 mg / dL (7mmol / L) on at least two occasions or the presence of symptoms with a casual plasma glucose ≥ 200 mg / dL (11.1 mmol / L) on two subsequent days [16];
- patients with urinary tract obstruction diagnosed on the basis of history, physical examination and ultrasonographic findings;
- patients in clinical heart failure because deterioration in kidney function could have occurred as a result of decreased cardiac output with subsequent decrease in kidney perfusion;
- patients with hypothyroidism or hyperthyroidism. The exclusion of thyroid disease was based on history and physical examination findings only;
- vegans because the vegetarian diet causes decreased glomerular filtration rate and
- patients who refused to give consent to be part of the study.

Blood pressure (BP) was taken using the mercury sphygmomanometer with appropriate cuff sizes. Blood pressure was taken after allowing at least 5 minutes rest and after ensuring that patients had not taken coffee or smoked cigarette within 30 minutes of taking BP. Systolic BP and DBP were taken as Korotkoff's sounds I and V respectively [17]. The BP readings were recorded to the nearest 2 mm Hg. Three BP readings were taken at 2 minutes interval and the average reading was calculated. The average reading was used for statistical analysis. Hypertension was defined by systolic blood pressure (SBP) ≥ 140 mm Hg and / or diastolic blood pressure (DBP) ≥ 90 mm Hg [18].

Patients' demographics were based on self-reported age, sex and educational status. Current history of smoking and alcohol intake, family history of hypertension and chronic kidney disease / failure was elicited and recorded. Each patient had his / her weight (in kg) checked in light clothing with the shoes off and the height (in metres) measured. The body mass index (BMI) was calculated from weight (kg) / height^2 (m^2). Each patient underwent physical examination. The renal arteries were auscultated for bruit. The thyroid gland was examined and the abdomen examined for enlarged kidneys and masses.

Kidney function was assessed by estimating glomerular filtration rate (GFR) with the Modification

of Diet in Renal Disease (MDRD) formula [12,19]. Estimated GFR = 186.3 × (serum creatinine)$^{-1.154}$ × age$^{-0.203}$ × (0.742 for woman) × (1.21 if African American).

Estimated GFR (eGFR) was classified into 5 categories according to the Kidney Disease Outcomes Qualitative Initiative (KDOQI) as follows: GFR < 15 mL / min (stage 5); 15 – 29.99 mL / min (stage 4); 30 – 59.99 mL / min (stage 3); 60 – 89.99 mL / min (stage 2); ≥ 90 mL / min (stage 1) [12]. Individuals with eGFR < 60 mL / min were classified as having decreased kidney function. This cut-off point was chosen to define decreased kidney function because a GFR of < 60 mL / min is abnormal in any population including the elderly [12].

Statistical analysis

Continuous variables were summarized as means ± standard deviation (S.D) and categorical variables were displayed as percentages. Differences between means were assessed using the student's t test and association between categorical variables by chi-square test. Logistic regression was used to correct for confounding variables. Statistical significance was considered at $p < 0.05$. Microsoft Excel 2003 (Microsoft Corp, Redmond, WA) and SPSS 11.0 (SPSS Inc, Chicago, IL) were used for data analysis.

Results

The baseline characteristics of the study population are as shown in table 1. The study population consisted of 63 males (44.1 %) and 80 females (55.9 %). The mean age of the study population was 55.59 ± 10.99 years. The females were significantly older than the males (57.79 ± 11.05 vs. 52.79 ± 10.34 yrs, $P = 0.007$) and had significantly higher BMI (27.78 ± 6.68 vs. 25.01 ± 3.30 kg / m^2, $p = 0.003$). The males had a non-significantly higher mean DBP when compared to females (112.79 ± 17.20 vs. 107.83 ± 14.23 mm Hg, $P = 0.061$) and a slightly lower mean SBP (174.68 ± 28.07 vs. 175.90 ± 25.77 mm Hg, $P = 0.788$).

The distribution of the eGFR is as shown in figure 1. Six (4.2 %), 27 (18.9 %), 83 (58.0 %), and 27 (18.9 %) subjects can be classified into stage 4, 3, 2, and 1 respectively. Thus, 33 patients (23.1 %) have eGFR < 60 mL / min and can be said to have decreased kidney function. The mean GFR of the males, females and the study population were 72.23 ± 20.13, 71.89 ± 23.57 and 72.04 ± 22.05 mL / min respectively. There was no statistically significant difference in the mean eGFR of the males compared to females ($P = 0.927$).

Table 1: Baseline characteristics of the study population

Characteristics	Male (%)	Female (%)	Total (%)
Gender	63 (44.1)	80 (55.9)	143 (100)
Educational status			
No formal education	11 (17.5)	42 (52.5)	53 (37.1)
Formal education	52 (72.5)	38 (47.5)	90 (62.9)
Mean age (years)	52.79 ± 10.34	57.79 ± 11.05	55.59 ± 10.99
Mean systolic blood pressure (mm Hg)	174.68 ± 28.07	175.90 ± 25.77	175.36 ± 26.72
Mean diastolic blood pressure (mm Hg)	112.79 ± 17.20	107.83 ± 14.23	110.01 ± 15.74
Weight (kg)	71.66 ± 10.34	70.01 ± 17.51	70.74 ± 14.76

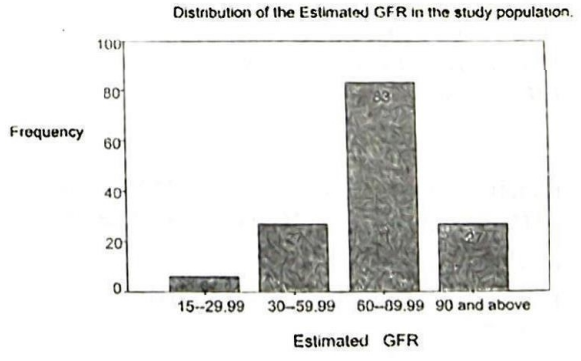

Fig. 1:

Table 2 shows the determinants of decreased kidney function. The prevalence of decreased kidney function was higher in females compared to males (26.3 % vs. 19.0 %) though the difference was not statistically significant ($X^2 = 1.030$, $P = 0.31$, OR = 1.513, 95 % CI = 0.678 – 3.374). The patients with decreased kidney function were significantly older

Table 2: Determinants of reduced kidney function in the study population

Characteristics	Number of patients with eGFR < 60 mL / min (%)	Number of patients with eGFR ≥ 60 mL / min (%)	P value
Gender			
Male	12 (19.0)	51 (81.0)	0.31
Female	21 (26.3)	59 (73.7)	
Educational status			
No formal education	22 (41.5)	31 (58.5)	0.0001
Had formal education	11 (12.2)	79 (87.8)	
Mean age ± SD (years)	63.55 ± 10.40	53.20 ± 10.03	0.000
Mean SBP ± SD (mm Hg)	188.67 ± 29.01	171.37 ± 24.77	0.001
Mean DBP ± SD (mm Hg)	117.70 ± 18.88	107.71 ± 13.96	0.001
Mean BMI ± SD (kg / m^2)	23.11 ± 3.86	27.59 ± 5.65	0.0001

SBP = systolic blood pressure
DBP = diastolic blood pressure
BMI = body mass index

Table 3: Logistic Regression of GFR outcome and the clinical correlates

Model	Unstandardized coefficients ß	Standard error	Standardized coefficients	t	significance
Constant	101.944	15.978		6.380	0.000
Age	- 0.958	0.143	- 0.478	-6.705	0.000
SBP	-9.4 E-02	0.065	-0.114	-1.438	0.153
DBP	-0.110	0.110	-0.078	-0.994	0.322
Edu. Status	0.873	1.315	0.047	0.664	0.508
BMI	1.876	0.230	0.478	8.156	0.000

SBP – systolic blood pressure
DBP – diastolic blood pressure
Edu. Status – educational status
BMI – body mass index

than those without decreased kidney function (63.55 ± 10.40 vs. 53.20 ± 10.03 years, T = 26.552, p = 0.000). Patients with decreased kidney function also had significantly higher SBP (188.67 ± 29.01 vs. 171.37 ± 24.77 mm Hg, t = 11.413, P = 0.001), and significantly higher DBP (117.70 ± 18.88 vs. 107.71 ± 13.96 mm Hg, P = 0.001). The prevalence of decreased kidney function was significantly higher in patients with no formal education when compared with those with formal education (66.7 % vs. 33.33 %, OR – 5.097; 95 % CI – 2.21 – 11.74, P = 0.0001). However, patients who had no formal education were significantly older than those with formal education (63.64 ± 9.37 vs. 50.84 ± 8.94 years, P = 0.0001) and had non-significantly higher SBP (177.96 ± 27.77 vs. 173.83 ± 26.12 mm Hg, P = 0.374) and lower DBP (107.92 ± 16.12 vs. 112.24 ± 15.48 mm Hg, P = 0.224). After correcting for age and blood pressure levels as confounding factors, there was no statistically significant difference in the prevalence of decreased kidney function between those with formal education and those without formal education ($P > 0.05$).

Discussion

This study showed that decreased kidney function was present in 23.1 % of newly diagnosed hypertensive patients. These patients thus stand a higher risk of faster progression of kidney disease.

chronic kidney failure, congestive cardiac failure and other cardiovascular complications and death.

Patients with decreased kidney function had significantly higher SBP and DBP than those without kidney function on univariate analysis. This finding agrees with findings from many studies which showed a strong, graded increased risk of CKD with increasing levels of SBP and DBP [20,21]. The mechanisms underlying kidney injury in hypertension though not completely defined include glomerular ischaemia secondary to vascular narrowing, glomerulosclerosis due to intracapillary hypertension and interstitial fibrosis [22,23].

Following regression analysis, SBP and DBP were not significantly associated with decreased kidney function. Though this finding appears unusual, not all studies have shown an association between blood pressure levels and decreased kidney function. Experimental and clinical studies have shown that the severity of blood pressure does not always predict the subsequent development of nephropathy or deterioration in kidney function [21,23]. In the Hypertension Detection and Follow-up Program study, renal function was found to decline in some patients despite optimal antihypertensive therapy [24]. Also, Klag *et al.* documented increase in the relative risk of chronic kidney failure in patients with BP levels in the high-normal range [20]. This non-association of severity of BP levels with CKD led to the concept of renal (kidney) susceptibility gene, that is, an appropriate genetic background needs to be present for the effect of sustained BP on kidney function to become manifest [22,25]. This concept of renal susceptibility gene is also supported in clinical studies by the strong familial occurrence of chronic kidney failure in hypertensive nephrosclerosis [26-28]. In this study, none of the subjects gave a family history of CKF. However, it must be borne in mind that the cause of death is not always known or investigated in our environment.

Lower socioeconomic status has been associated with CKF in all racial groups [29]. The concept of socioeconomic status can be measured by two indicators namely income and educational status. Education may, however, be a better indicator since the level of education changes little after young adulthood whereas progressive kidney insufficiency may have reduced the income-earning capacity of CKF patients [29]. In this study, decreased kidney function was significantly associated with no formal education on univariate analysis. After correcting for confounding factors, the effect of level of education on kidney function was no longer statistically significant. The patients with decreased kidney function were significantly older and less educated than those without decreased kidney function. There is a likelihood that the level of education could have influenced the time of presentation of the patients in the hospital and this may explain why those with decreased kidney function were significantly older.

Patients with decreased kidney function have statistically significant lower BMI than those without decreased kidney function. The finding appears incongruous because GFR is expected to fall with prolonged overweight / obesity [30,31]. This is because with prolonged obesity, increases in arterial pressure from impaired natriuresis, renal vasodilatation and glomerular hyperfiltration, neurohormonal activation and metabolic changes are expected to cause glomerular injury and further impairment of renal – pressure natriuresis resulting in more severe hypertension and a loss of kidney function [30,31]. One plausible explanation for this finding is that decreased kidney function could have resulted in some degree of nutritional disturbance with consequent reduction in the BMI [32]. Available evidence suggests a chronic inflammatory state in patients with GFR < 60 mL / min as shown by increased concentrations of pro-inflammatory cytokines and acute phase reactants [33,34]. The metabolic and nutritional effects of chronic inflammation include anorexia, increased skeletal muscle protein breakdown, increased whole body protein catabolism, cytokine-mediated hyper-metabolism and disruption of the growth hormone and insulin-like growth factor 1 axis leading to decreased anabolism [33,34].

This study has some limitations. First, it was carried out in a tertiary health care centre, so the findings may not apply to the population as a whole. Second, GFR was estimated using the MDRD formula which may not be as accurate as using isotopic markers [35,36]. However, equations to estimate GFR give more valid estimates of GFR than serum creatinine alone; are cheaper and more practical than urine collections [12]. Third, thyroid function test was not done; so patients with sub-clinical hypothyroidism or hyperthyroidism could have been missed. Lastly, other markers of

malnutrition such as serum albumin were not assessed in these patients. This could have helped to determine whether decreased BMI associated with reduced kidney function was due to malnutrition or not.

In conclusion, decreased kidney function was present in 23.1 % of the patients. These patients stand a higher risk of faster progression of kidney disease, chronic kidney failure and cardiovascular complications. This finding underscores the need to improve the awareness of hypertension in the population since this will lead to early detection and subsequent commencement of therapy with attendant reduction in kidney and cardiovascular mortality.

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Recieved: 27/10/06
Accepted: 03/04/07