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TARGET ORGAN DAMAGE AND ASSOCIATED CLINICAL CONDITIONS IN NEWLY DIAGNOSED HYPERTENSIVES ATTENDING A TERTIARY HEALTH FACILITY

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ABSTRACT

Background: Despite the ease of detecting and making a diagnosis of hypertension, various population surveys have shown low awareness and treatment rates of hypertension. Failure to detect and make a diagnosis of hypertension leads to late presentation and institution of treatment with consequent development of target organ damage (TOD) and associated clinical conditions (ACC) which in turn are associated with increased cost of treatment, morbidity and mortality.

Objective: This study was aimed at determining the presence and severity of TOD and ACC in newly diagnosed hypertensives with a view to ascertaining the magnitude of the problem.

Method: The study was carried out at Ladoke Akintola University of Technology Teaching Hospital Osogbo, Nigeria. Target organ damage (TOD) and associated clinical conditions (ACC) were determined in successive newly diagnosed hypertensives that presented at the centre during the study period.

Result: Of 147 newly diagnosed hypertensives seen at Ladoke Akintola University of Technology Teaching Hospital Osogbo, Nigeria, TOD and ACC were found in 98 (66.7 %). The most prevalent TOD and ACC were LVH (42.2 %), diabetes mellitus (14.3 %), CVD (10.9 %) and heart failure (8.8 %). Patients with TOD and ACC were significantly older (p = 0.028), had significantly higher SBP (p = 0.003), higher DBP (p = 0.022) and significantly lower BMI (p = 0.046) when compared with patients without TOD and ACC.

Conclusion: This study showed presence of TOD and ACC in two-thirds of newly diagnosed hypertensives. This underscores the need for improvement in the awareness, detection and treatment of hypertension in order to prevent TOD and ACC.

Key Words: Target organ damage, Associated clinical conditions, Newly diagnosed hypertensives

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INTRODUCTION

Systemic hypertension is an important medical and public health issue affecting one billion people worldwide and accounting for approximately 7.1 million deaths per year.[1] It is an important risk factor for cardiovascular and renal diseases.[2,3] The prevalence rate of hypertension in Nigeria ranges from 7 20 % from published studies.[4-6] Though it is relatively easy to detect and make a diagnosis of hypertension, population surveys have documented low awareness rates in various countries.[4,7,8] The level of awareness of hypertension in Nigeria according to the National Non-communicable Survey was 33.8 %.[4] The import of this low awareness is late presentation to the hospital for treatment, with attendant development of target organ damage (TOD) and associated clinical condition (ACC) which in turn is associated with increased morbidity and mortality. For example, the one year mortality of patients with symptomatic heart failure was 45 %.[9, 10] Also, the expected life expectancy of patients with chronic renal failure treated by dialysis was far shorter than the age-matched general population with rates varying (depending on sex and race) from 7.1 to 11.5 years for patients aged 40 to 44 years and from 2.7 to 3.9 years for patients aged 60 to 64 years.[11] The cost of treatment following the development of TOD and ACC is also exorbitant. It was estimated in 1997 that $5,501.00 was spent for every hospital discharge diagnosis of heart failure and another $1,742.00 per month was required to care for each patient after

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discharge.[12] In view of the foregoing, we have determined the presence and severity of TOD and ACC in newly diagnosed hypertensives presenting in a tertiary health care centre with a view to ascertaining the magnitude of the problem.

SUBJECTS AND METHODS

This was a prospective study carried out at Ladoke Akintola University Teaching Hospital (LTH), Osogbo, in Southwest Nigeria. The study period was from January 2004 to February 2005. The study population consisted of 147 patients recruited after an informed consent had been given by the individual patient or the next of kin.

Inclusion Criteria: Included in the study were consecutively newly diagnosed patients with hypertension who had not been on any anti-hypertensive drugs or had been on anti-hypertensives for less than one week. Blood pressure (BP) was taken using the mercury sphygmomanometer with appropriate cuff sizes and according to standardized protocols.[13] A patient was considered hypertensive if he or she had persistently elevated systolic blood pressure (SBP) = 140 mm Hg and / or diastolic blood pressure (DBP) = 90 mm Hg.[14,15] Target organ damage and ACC were as outlined in the 2003 World Health Organization / International Society of Hypertension Statement on the management of hypertension.[14]

Exclusion criteria: Excluded from the study were patients who had earlier been diagnosed as hypertensive and had been on drugs but discontinued the drugs and later represented; patients with primary kidney disease as suggested by the history, active urinary sediments and renal ultrasonography; patients who refused consent and those who died before assessment of TOD and ACC was concluded.

Data Collection: A structured questionnaire was used to obtain information such as age, sex, educational status, family history of hypertension, history of alcohol consumption and cigarette smoking.

Clinical Evaluation: A detailed history was obtained from each patient or close relatives when patient was unable to give the history to determine the circumstances surrounding the diagnosis and the presence of features of TOD / ACC. The weight (in kilograms) of each patient was taken in light clothing with the shoes off and height (in metres). The body mass index (BMI) was calculated from weight / height^2 (kg / m^2). In patients with heart failure, the weight used in calculating the BMI was the weight obtained after the fluid retention had resolved. Overweight and obesity were defined as BMI of 25 29.9 kg / m^2 and = 30 kg / m^2 respectively.

Each patient underwent physical examination by the attending physicians (who are contributing authors) looking for features of heart failure, left ventricular hypertrophy (LVH), cerebrovascular disease (CVD) and renal failure. The carotid, renal and femoral arteries were auscultated for bruits. The thyroid gland was examined for enlargement and bruit. The abdomen was examined for enlarged kidneys, masses, distended urinary bladder. The lower extremities were examined for oedema and pulses. The blood pressure at first contact was noted. In the case of patients who had been started on anti-hypertensives before referral to the Medical Outpatient Department of the hospital, the referring doctor or health personnel was contacted to know the BP of the patients before commencement of anti-hypertensive if this was not stated in the referral letter. Fundoscopy was done to determine the presence and severity of hypertensive retinal changes.

Investigations: Investigations done on each patient included urinalysis, urine microscopy for cells and casts, serum electrolytes, urea and creatinine, abdominal ultrasonography, fasting plasma glucose and resting 12 lead electrocardiography (ECG). Glomerular filtration rate (GFR) was estimated from the Cockcroft Gault formula[16]:

GFR = (140 age {years}) / serum creatinine (mg / dL) × (weight (kg) / 72) × 0.85 (if female) × BSA / 1.73 m^2 (where BSA is the body surface area, estimated using the formula[17]: BSA (m^2) = 0.20247 × height (m)$^{0.725}$ × weight (kg)$^{0.425}$

The Cockcroft Gault formula was used to estimate GFR in this study because earlier studies from Africa have shown that GFR estimated using this formula showed a good correlation with measured GFR using endogenous creatinine clearance and ^{51}Cr-ethylenediaminetetra-acetic acid (^{51}Cr-EDTA).[18,19]

Each patient had serum creatinine and weight rechecked three months following the first presentation and GFR was re estimated. Only patients with estimated GFR persistently < 60 mL / min or those with persistent dipstick positive proteinuria in the absence of urinary tract infection as determined by urine culture were classified as having chronic kidney disease CKD.[20]

Clinical heart failure was diagnosed on the basis of clinical features and chest x-ray findings. Left ventricular hypertrophy (LVH) was assessed with the 12-lead ECG.[21] In view of the limitations of using Keith-Wagener-Barker grade I and II hypertensive retinopathy as a marker of TOD in hypertension[22], grade III (i.e. the presence of exudates and haemorrhages) and grade IV (i.e. grade III changes

and papilloedema) were used as evidence of TOD in the eyes. The presence of diabetes mellitus (DM) was defined by persistent fasting plasma glucose (FPG) = 126 mg / dL (7.0 mmol / L).[23]

Target organ damage was simply taken as present or absent. The number of TOD and ACC was also noted.

Ethical Approval: Ethical approval was obtained for the study from Ladoke Akintola University of Technology / Ladoke Akintola University Teaching Hospital Ethical Committee.

Statistical Analysis

Continuous and categorical variables were displayed as means ± standard deviation (S.D) and percentages respectively. The student's t test was used to assess differences between means. Differences between categorical variables were analyzed by Chi-square test with Fisher's exact correction applied as appropriate. Differences between groups were analyzed by analysis of variance (ANOVA). Statistical significance was considered at $p < 0.05$.

RESULTS

The baseline characteristics of the study population are as shown in table 1. One hundred and fifty four newly diagnosed hypertensives were seen during the study period. Of these, three patients died before assessment of TOD and ACC could be completed and four patients were lost to follow up so their serum creatinine and estimated GFR couldnot be determined three months after their first presentation. Of the remaining 147 patients, 65 (44.2 %) were males and 82 (55.8 %) were females giving a female to male ratio of 1.26:1. The larger Population of females in the study population reflected the hospitals' attendance during the study period. The female to male hospitals' attendance rate during the study period was 1.3 1.4:1. The mean age of the study population was 55.78 ± 10.91 years.

Ninety eight patients (66.7 %) had TOD and ACC while 49 (33.3 %) had no TOD and ACC. Fifty seven (38.8 %), 27 (18.4 %), and 14 (9.5 %) patients had one, two, and three TOD / ACC respectively. The gender difference in the prevalence of TOD / ACC was not statistically significant (males 66.7 %, females 65.9 % ($p = 0.861$).

The distribution of the various TOD / ACC is as shown in table 2. The most prevalent TOD / ACC were LVH (42.2 %). No patient had acute myocardial infarction during the study period.

Table 3 shows the characteristics of patients with and without TOD / ACC. Patients with TOD / ACC were significantly older (55.17 ± 11.00 vs. 52.98 ± 10.27 years, $p = 0.028$); had significantly higher SBP at diagnosis (180.80 ± 28.59 vs. 166.80 ± 22.70 mm Hg, $p = 0.003$); significantly higher DBP at diagnosis (112.10 ± 17.35 vs. 105.71 ± 12.17 mm Hg, $p = 0.022$) and significantly higher pulse pressure (68.69 ± 20.94 vs. 61.08 ± 19.86 mm Hg, $p = 0.036$). On the other hand, patients with no TOD / ACC had significantly higher BMI when compared with patients with TOD / ACC (27.86 ± 5.91 vs. 25.88 ± 5.36 kg /m^2, $p = 0.046$). Only one patient gave a history of current smoking and this number was too small to be subjected to statistical analysis.

Table 1. **Baseline Characteristics of the Study Population**

Variable	Male (%)	Female (%)	Total (%)
Number of patients	65 (44.2)	82 (55.8)	147 (100)
Mean age ± SD (years)	53.12 ± 10.36	57.88 ± 10.94	55.78 ± 10.91
Educational status			
Nil	12 (18.5)	41 (50)	53 (36.1)
Primary	10 (15.4)	15 (18.3)	25 (17.0)
Secondary	19 (29.2)	16 (19.5)	35 (23.8)
Post-secondary	24 (36.9)	10 (12.2)	34 (23.1)
Mean SBP ± SD (mm Hg)	176.29 ± 30.07	176.00 ± 25.51	176.13 ± 27.52
Mean DBP ± SD (mm Hg)	113.23 ± 17.58	107.39 ± 14.32	109.97 ± 16.06
PP ± SD (mm Hg)	63.06 ± 21.27	68.61 ± 20.28	66.16 ± 20.83
BMI (kg / m^2)			
< 25.0	30 (46.2)	30 (36.6)	60 (40.8)
25.0 29.9	29 (44.6)	24 (29.3)	53 (36.1)
≥ 30.0	4 (6.2)	26 (31.7)	30 (20.4)

Key to Table.
SD standard deviation
SBP systolic blood pressure
DBP diastolic blood pressure
PP pulse pressure
BMI body mass index

Table 2. **Prevalence of Target Organ Damage and Associated Clinical Condition in Newly Diagnosed Hypertensives.**

TOD / ACC	Male (%)	Female (%)	Total (%)
Left ventricular hypertrophy	31 (47.7)	31 (37.8)	62 (42.2)
Chronic kidney disease	11 (16.9)	24 (29.3)	35 (23.8)
Presence of diabetes mellitus	11 (16.9)	10 (12.2)	21 (14.3)
Cerebrovascular disease	6 (9.2)	10 (12.2)	16 (10.9)
Symptomatic heart failure	7 (10.8)	6 (7.3)	13 (8.8)
Advanced retinopathy	3 (4.6)	1 (1.2)	4 (2.7)
Transient ischaemic attack	1 (1.5)	1 (1.2)	2 (1.4)

Table 3. **Characteristics of Patients with and without Target Organ Damage and Associated Clinical Conditions**

Variable	Presence of TOD / ACC (%)	Absence of TOD / ACC (%)	p value
Gender			
Male	44 (67.7)	21 (32.3)	0.861
Female	54 (65.9)	28 (34.1)	
Age ± SD (years)	57.17 ± 11.00	52.98 ± 10.27	0.028
Mean SBP ± SD (mm Hg)	180.80 ± 28.59	166.80 ±22.70	0.003
Mean DBP ± SD (mm Hg)	112.10 ± 17.35	105.71 ± 12.17	0.022
Mean PP ± SD (mm Hg)	68.69 ± 20.94	61.08 ± 19.86	0.036
Mean BMI ± SD (kg / m^2)	25.88 ± 5.36	27.86 ± 5.91	0.046
Mean weight ± SD (kg)	68.96 ± 14.13	74.13 ± 15.49	0.047
Family history of hypertension	6 (6.1)	7 (14.3)	0.126
History of alcohol intake	17 (17.3)	4 (8.2)	0.210

DISCUSSION

This study showed that TOD / ACC were present in two-thirds of newly diagnosed hypertensives. This probably reflects unawareness of hypertension on the part of these patients with consequent late presentation since the development of TOD / ACC is partly determined by the severity and duration of hypertension. The prevalence of TOD / ACC was higher in males compared to females. Similar findings have been documented in hypertensives on treatment.[24, 25] Reasons put forward to explain this higher prevalence of TOD / ACC in males included a greater severity of hypertension in males when compared to females and an inherent proneness in males to develop certain TOD / ACC. In this study, when compared to females, males had comparable mean SBP (176.29 ± 30.07 vs 176.00 mm Hg, p = 0.949) but significantly higher DBP (113.23 ± 17.58 vs 107.39 ± 14.32, p = 0.028). Patients with TOD / ACC had significantly higher SBP and DBP compared with those without TOD / ACC. This is not surprising because TOD / ACC is partly determined by the level of BP. It is, however, difficult to explain the higher BMI in patients without TOD / ACC when compared with those who had TOD / ACC.

The most prevalent TOD in the patients was LVH which was seen in 42.2 % of patients. The prevalence of LVH in this study was comparable to 43.3 % obtained by Familoni et al.[25] though the latter study looked at TOD in treated hypertensives. The implication of this high prevalence of LVH is increased cardiovascular morbidity and mortality particularly if this complication is unattended to. However, the use of anti-hypertensive drugs, particularly the use of agents such as angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers or diuretics to control BP to goal values, can help with regression of LVH with subsequent reduction in cardiovascular mortality.[26,27] Diabetes mellitus (DM) was concomitantly detected in 21 patients (14.3 %) of newly diagnosed hypertensives. This prevalence of DM is much higher than 2.8 %

Reported in the National Survey of Non communicable Diseases in Nigeria.[4] It, however, is in keeping with a previous study that has shown an increased prevalence of diabetes in patients with hypertension.[28] Gress et al[28] in a prospective cohort study that included 12550 adults showed that the development of type 2 diabetes was almost 2.5 times as likely in persons with hypertension as in their normotensive counterparts. The underlying reason for the increased prevalence of diabetes in patients with hypertension is still controversial but insulin resistance has been proposed as the underlying pathogenetic mechanism.[29] Symptomatic heart failure was seen in 8.8 % of the patients. Hypertension remains the leading cause of heart failure in Nigeria. The presence of hypertension increases the risk for heart failure by 2- to 3-fold.[9] The presence of heart failure is associated with a dismal prognosis with a one-year mortality of approximately 45 %.[9,10] Cerebrovascular disease was seen in 16 (10.9 %) patients. Earlier reports have shown that hypertension remains a major risk factor for stroke in Nigeria and other African countries being responsible for 60 92 % of patients with cerebral haemorrhage and 33 62 % of those with non-embolic cerebral infarction.[30] No patient had acute myocardial infarction (MI) during the study period. This is not too surprising because reports have shown low incidence of MI in Nigerians. However, going by the report of a slight increase in the incidence of myocardial infarction in Nigerians from 1:20000 to 1:10000 in the hospital population,[31,32] attempts should be made at controlling risk factors such as hypertension, diabetes, hyperlipidaemia and encouraging healthy eating habits and regular exercise in order to prevent increased incidence of MI in the population.

This study had some limitations. First, LVH was assessed by ECG which is not as sensitive and specific as echocardiography. However, LVH by ECG has been shown to be associated with increased cardiovascular morbidity and mortality. Second, there is likelihood that few patients with intrinsic kidney disease may have been included in the study because no kidney biopsy was done in the patient. This was because of the ethical issues involved in taking kidney biopsy from all patients with hypertension. However, the result of the renal biopsy performed in the pilot patients in the African American Study on Kidney disease and hypertension (AASK) would give credence to our approach in diagnosing hypertensive nephrosclerosis.[33] Third, diagnosis of CVD was based on clinical diagnosis because not all patients could afford computerized tomography. Thus, misdiagnosis of CVD is possible.[34] Fourth, the high prevalence of TOD / ACC found in this study population may not be representative of the newly diagnosed hypertensive population in the community since patients with mild hypertension (and hence lower prevalence of TOD / ACC) may not be referred to tertiary centres for care. Finally, carotid wall thickening or atherosclerotic plaque assessment was not done.

In summary, this study showed that two-thirds of newly diagnosed hypertensives have TOD / ACC. It is recommended from the findings of this study that blood pressure screening programs in the community should be put in place and sustained. This will ensure early detection and institution of treatment which in turn will reduce target organ damage and associated clinical conditions from hypertension.

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