Reported Adherence to Antihypertensive Treatment and Outcome at Postmortem in Southwestern Nigerians

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Abstract

Background: Systemic hypertension is referred to as a silent killer. Knowledge of disease and religious use of medication could mitigate against complications in hypertensives. This study evaluated outcome among decedent essential hypertensive patients in southwestern Nigeria in relation to their compliance with prescribed antihypertensive medication. **Materials and Methods:** This is a 10-year retrospective review of routine postmortem data. Archival postmortem records from January 1, 2008 to December 31, 2017 in the Department of Pathology, University College Hospital, Ibadan, Nigeria, were reviewed. Data extracted from the records included age, gender, knowledge of hypertension status, systolic and diastolic blood pressure at time of diagnosis, reported adherence to medications, complications of systemic hypertension, duration of survival from diagnosis to demise, cause of death, body length, and heart weight at autopsy. Descriptive, Students t-test, Chi-square test, Pearson correlation and Cox proportional-hazards model statistics was conducted using SPSS version 20 (IBM SPSS Statistics for windows, IBM Corp., Armonk, N.Y., USA). $P < 0.05$ was considered significant. **Results:** Eighty-one cases met the inclusion criteria, consisting of 60 males and 21 females with overall mean age of 55.65 ± 12.1 years. Seventy-five (91.7%) cases were known hypertensives prior to admission or demise while 6 (8.3%) were not known hypertensives. The duration of survival from diagnosis to death ranged from 1-month (0.08 years) to 31 years with overall mean duration of 5.2 years. Fifty-two (63.4%) of the 75 known hypertensive cases had documented medication compliance. Medication noncompliant cases had lower mean survival interval (5 vs. 8 years), died younger (53.5 ± 10.8 years vs. 54.8 ± 15.5 years), had higher mean blood pressures (systolic blood pressures: 197 ± 45.8 mmHg vs. 180 ± 55.4 mmHg; diastolic blood pressures: 117 ± 27.2 mmHg vs. 101 ± 32.8 mmHg) and heavier heart weights (476 ± 142 g vs. 390.8 ± 107.6 g). However, only the difference in heart weight was statistically significant ($P < 0.036$). Age and mean systolic blood pressures were correlated with interval from diagnosis to death ($r = 0.5, P < 0.000; r = -0.4, P < 0.017$, respectively). Death from complications of hypertension and all-cause mortality occurred with higher frequencies among medication noncompliant cases (40 vs. 12). **Conclusion:** Noncompliance with antihypertensive medication is associated with more cardiovascular and all-cause mortality among Southwestern Nigerians with essential hypertension.

Keywords: Antihypertensives, cardiovascular events, Nigeria, postmortem

INTRODUCTION

Systemic hypertension affects about 1 billion persons globally and it is and its complications account for about 9.4 million deaths worldwide annually.[1] The African continent has the highest prevalence of systemic hypertension globally with 46% of adults 25 years and above affected, the lowest prevalence occurring in the Americas at 35%.[1] Data from studies among Nigerians aged 18 years and above have documented crude prevalence ranging widely between 2.1% and 47.2%.[2] The risk of dying from systemic hypertension-related complications in low- and middle-income countries is about double that among high-income countries with about 25% of these deaths occurring in individuals younger than 60 years in the low and middle income countries compared to 7% in the high-income countries.[3] A study among hypertensives in America showed that mortality due to circulatory system disease was significantly higher in blacks than whites.[4] Some of the explanations for this worrisome disparity include low awareness of an individual's hypertension status,[5] poor compliance with antihypertensive medications,[6] and an inadequate understanding of the

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pathological and hemodynamic changes that had already taken place in individual patient before diagnosis to guide appropriate therapy.[7] Individuals who don't know their systemic hypertension status and those who are poorly compliant with medications after being diagnosed are at a greater risk of cardiovascular complications. Oladapo *et al.* in the course of examining 2000 apparently healthy Yoruba adults between 18 and 64 years who lived in a rural community in South-Western Nigeria discovered that 415 of them were hypertensive, and 179 (43.1%) of these 415 hypertensives already had target organ damage such as hypertensive heart disease (HHD), renal disease, hypertensive retinopathy and stroke.[8] Another study by Akpa and Wokoma found that 25% of newly presenting patients already had evidence of left ventricular hypertrophy on electrocardiography[9] suggesting that among Nigerians, evidence of longstanding hypertension often precedes diagnosis and this probably results in "premature deaths, disability, personal and family disruptions, and loss of income due to health care expenditures."[1,9] Predictors of morbidity and mortality include elevated mean blood pressure, age, increased body mass index, poor compliance with antihypertensive treatment among others.[3,10-13] Autopsy studies evaluating the effect of compliance with antihypertensive treatment and duration of survival from diagnosis to death at postmortem are few.[14] This study aims to provide data on postmortem findings of systemic hypertension disease among Nigerians.

MATERIALS AND METHODS

This retrospective study is a 10-year review of routine postmortem data. Autopsy records and summarized clinical notes of decedents archived at the Department of Pathology, University College Hospital, Ibadan, from January 2008 to December 2017 were reviewed and those that met the inclusion criteria were included in the study. Inclusion criteria included age of 20 years and above, documented awareness of hypertension status or otherwise prior to admission or death, and autopsy findings in keeping with hypertension whether or not the cause of death is related to hypertensive disease. Decedents younger than 20 years, those with secondary hypertension, and nonhypertensives with no autopsy features of hypertension were excluded from the study. This study was conducted in compliance with the guidelines of the Declaration of Helsinki on biomedical research in human subjects. Confidentiality of the identity of the patients and personal health information was maintained. All autopsies were carried out upon obtaining consent from the deceased's relatives. Demographic and clinical data of the decedents retrieved included age, gender, body length, occupation, knowledge of hypertension status (yes/no), duration of hypertension from diagnosis to death, previous complications, history of compliance with medications (yes/no), systolic and diastolic blood pressure, and cause of death. The heart weight at autopsy of the decedents was also documented. The weight of the heart recorded was the absolute weight at the time of autopsy. Blood pressure recordings used in this study

was that documented at the time the patient presented in the hospital just prior to the time they died. This was therefore a single measurement as most of these patients presented with hypertensive emergencies leading to their death. Causes of death were categorized into HHD, stroke (hemorrhagic and ischemic), ischemic heart disease (IHD), ruptured aortic aneurysm and others representing nonhypertensive disease-related deaths. HHD was defined according to International Classification of Disease that describes HHD with failure and HHD without failure.[15] Frequency statistics was used to examine proportions of males and females, age groups, awareness status, compliance to medication status and occupation distribution of the study population. Student's *t*-test and Pearson correlation statistics was used to test difference in means and correlations respectively between continuous variables such as age, heart weight, body length and survival interval from diagnosis, with drug compliance (Yes/No) as the comparison variable. Chi-square test statistic was used to test for association between survival interval and cause of death and between survival interval and age group. Cox proportional-hazards model was conducted to determine the time to fatal cardiovascular events among the participants. Level of significance was set at $P < 0.05$.

RESULTS

The demographics of the study population is as shown in Table 1. One hundred and seven cases of decedents with prior clinical diagnosis or autopsy findings with organ changes consistent with systemic hypertension were retrieved. Out of these, 26 cases had no documentation of knowledge about their hypertension status and were further excluded from

Table 1: Demographic characteristics of the study cases

Variable	Frequency (%)
Gender (*n*=81)	
Female	21 (25.6)
Male	60 (74.4)
Age group (years) (*n*=81)	
30-39	8 (9.9)
40-49	14 (17.3)
50-59	30 (37.0)
60-69	15 (18.5)
70-80	14 (17.3)
Awareness of hypertension status (*n*=81)	
Yes	75 (92.6)
No	6 (7.4)
Medication compliance (n=52)	
Yes	12 (23.1)
No	40 (76.9)
Occupation (*n*=81)	
Architect/engineer/civil servant	12 (14.8)
Trading/artisan	26
Teaching/driving	13
Student/unemployed	16
Unclassified	14

the study. Of the 81 cases that met the minimum criteria of documented hypertension status (Yes/No) and cause of death, there were 60 males and 21 females with overall mean age of 55.65 ± 12.1 years. The age group distribution of the participants is as shown in Table 1. None of the cases was <30 years of age. Seventy-five (92.6%) of cases were known hypertensives before admission or demise. Of these 75 known hypertensive cases, documented information on the duration of hypertension from diagnosis was available for 46 (61.3%) cases while information on compliance with antihypertensives was available for 52 (9.3%) cases (yes 12, no 42). The duration of survival from diagnosis to death ranged from 1 month (0.08 years) to 31 years with a crude mean duration of 5 years. Figure 1 shows the distribution of interval from diagnosis to death of the cases. HHD was the most common cause of death in this series [Figure 2], with mean heart weight of 436.11 ± 146.39 g.

We further analyzed the 52 cases that had documented information on whether or not they were compliant with medication and tested for difference in survival interval between antihypertensive medication compliant and noncompliant cases. The result showed that those noncompliant with antihypertensive medications had a mean survival interval of 5 years (compared to 8 years for medication compliant cases), had higher mean blood pressures and heavier heart weights [Table 2]. Cause of death from acute left ventricular failure (ALVF), congestive heart failure (CHF), hemorrhagic stroke, and HHD all occurred with higher frequencies among medication noncompliant cases (40 vs. 11) while a single case of ischemic cardiac events was seen in a drug compliant case.

Nine (17.3%) of the 52 cases had previous complications from hypertension but had a different cause of death. One case had retinal detachment and died of ALVF. Two cases had prior ischemic stroke but died of hemorrhagic stroke and aspiration pneumonitis each. A fourth case had CHF but died of pulmonary tuberculosis. The remaining five cases had chronic kidney disease but died of HHD with heart failure (three cases) and without heart failure (two cases). Seven (77.7%) of these nine cases were male.

There was a significant association between survival interval and age group ($P < 0.001$; Fisher exact test). Correlation

between age and survival interval from diagnosis to death was positive ($r = 0.5$, $P < 0.000$) while that between mean systolic blood pressure and survival interval was negative ($r = -0.4$, $P < 0.017$). Correlation between diastolic blood pressure, heart weight, body length each and survival interval was negative and nonsignificant. The observed significant relationship between age and systolic blood pressure was

Table 2: Comparison of mean of variables between antihypertensive medication compliant and noncompliant decedents

Variable	*n*	Antihypertensive medication compliance (mean±SD)		*P*
		Yes	No	
Age (years)	81	54.8±15.5	53.5±10.8	0.784
SBP (mmHg)	81	180±55.4	197±45.8	0.394
DBP (mmHg)	81	101±32.8	117±27.2	0.197
Body length (m)	81	1.7±0.09	1.6±0.28	0.303
Heart weight (g)	81	390.8±107.6	476±142	0.036*

SBP – Systolic blood pressure, DBP – Diastolic blood pressure, SD – Standard deviation. *The *P* value is less than 0.05. The medication non-compliant cases had significantly heavier heart weights
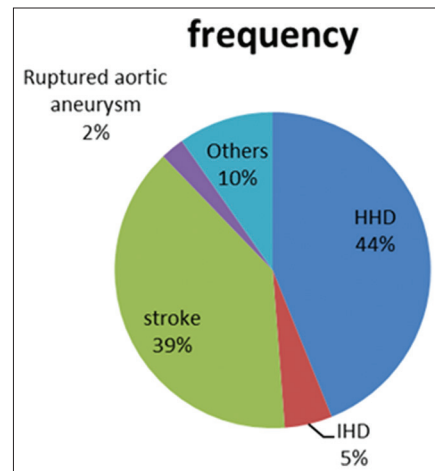
Table 3: Cox proportional-hazards regression showing predictors of time interval from diagnosis to adverse event

Variable	Hazard ratio	95% CI	*P*
Gender (male/female)	0.675	0.247-1.845	0.444
SBP (mmHg)	1.019	1.005-1.033	0.007*
DBP (mmHg)	0.992	0.974-1.009	0.353
Medication compliance (yes/no)	0.520	0.165-1.645	0.266
Heart weight (g)	1.000	0.998-1.003	0.751
Body length (m)	0.209	0.001-29.603	0.535
Age group (years)	0.940	0.892-0.990	0.018*

SBP – Systolic blood pressure, DBP – Diastolic blood pressure, CI – Confidence interval. *The p value is less than 0.05 showing that a younger age of onset of systemic hypertension is a strong predictor of adverse outcome
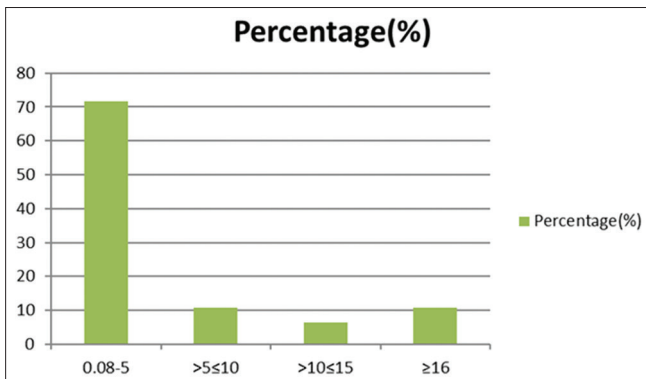
Figure 1: Duration of survival from diagnosis to death (years)

**Figure 2:** A pie chart illustrating the causes of death by proportion

subjected to Cox proportional-hazards modeling to test for the effect of confounding factors [Table 3]. Age and mean systolic blood pressure remained predictors of outcome although their effect was attenuated. Shown in Figure 3 is the cox hazard plots of the cumulative occurrence in time intervals between medication compliant and non-medication compliant cases. Overall fewer events were observed among compliant individuals than among non-compliant individuals. Additionally, all events occurred earlier among medications non-compliant cases.

DISCUSSION

The prevalence (77%) of lack of compliance with antihypertensive therapy reported in this study is higher than the 49% reported by Osamor and Owumi in southwest Nigeria.[6] Both study populations are similar, consisting predominantly of traders and artisans and could be influenced by similar cultural and socioeconomic factors. The population studied by the latter was a community health outpost volunteer cohort study group on hypertension and had participated in previous community based hypertension study.[6] They had therefore been previously educated on hypertension, hence the lower prevalence of lack of treatment compliance compared to our study. The authors suggested strongly that health education plays a key role in modifying attitude to disease.[6]

Despite the minimal difference in the mean age of medication compliant and non-compliant cases, The non-compliant cases had shorter survival interval from diagnosis. They also had higher mean systolic and diastolic blood pressure and had significantly heavier heart weights compared to the medication compliant cases.

The first 5 years of diagnosis might be a critical period in the management of newly diagnosed hypertensives as it was observed in this study that 71% of deaths occurred within this period. Reason(s) for the significant association between survival interval and age group is not clear given that the deaths were evenly distributed across the age groups.
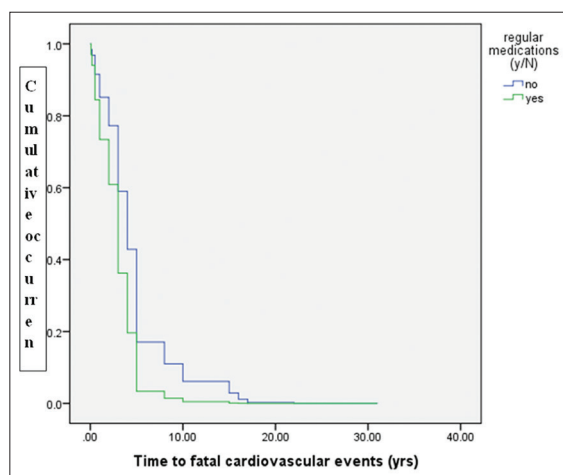
Figure 3: Cumulative occurrence of fatal cardiovascular events between medication compliant and noncompliant participants

Awareness of hypertension status by patients is a prerequisite for effective blood pressure control but in this study the realization that one is hypertensive did not translate to strict adherence with medications. This high level of awareness observed in this study could be accounted for by the fact that this was a hospital-based study and may not be representative of the population figures. Raji *et al*.[5] in their report from the Ibadan study of aging, a population based study found 22% prevalence of awareness of hypertension. However, there is data reporting 70% awareness among adults in the United States of America[3] which is similar to the finding in this present study.

The significant correlation between age group and systolic blood pressure but not diastolic blood pressure and survival interval agrees with the reports by Verdecchia *et al*.[16] though their study found nonsignificant effect of systolic blood pressure on multivariate analysis. Other studies have also shown significant effect of age, systolic and diastolic blood pressure on survival among essential hypertensive patients.[11] This finding suggests that uncontrolled hypertension leads to cardiovascular complications as shown by younger age at death and shorter interval from diagnosis of hypertension to death. This is further supported by the finding of more cardiovascular events as causes of mortality in the medication noncompliant cases except IHD which occurred predominantly among medication compliant cases. Seventeen percent of these cases also had prior complications from hypertension. Besides noncompliance to medication, obesity[5] and reduced drug efficacy[17] have been proposed as causes of poor blood pressure control among essential hypertensives. The occurrence of IHD predominantly among medication-compliant cases suggests a multifactorial cause of the condition besides hypertension.[18]

The difference in heart weights between medication compliant and noncompliant cases also suggests a causal effect of uncontrolled blood pressure in differential myocardial hypertrophy. Increased force of contraction of the affected heart could worsen the vascular endothelial damage and end-organ effects of hypertension and could be responsible for the high proportion of stroke seen in this study. It has been shown that blood pressure control with medicines and/or lifestyle modifications reduces morbidity and mortality from hypertension.[3,4] Countries that have achieved reduction in prevalence of hypertension and its complications have done so largely due to massive and intensive public health education and awareness.[1] More needs to be done in this environment regarding this.

Despite the difference in the proportion of medication compliant individuals in this study and that of Kolo *et al*.[12] in Northeastern Nigeria, both studies did not find a significant association between medication compliance and survival interval. This could partly be due to small sample size in both studies. The study by Kolo *et al*. was a prospective follow-up study with 36.4% drug compliance compared to 23% in this present study. Lawlor *et al*.[11] in their study of British

hypertensives observed that having a small percentage of participants with well controlled blood pressure among a large cohort would not permit a reasonable conclusion on the effect of treatment on outcomes and survival.

Contributors to poor adherence with medications could include nonregular attendance to clinic appointments, use of unorthodox medicines, lack of social support from family and friends, and lack of sustainable income.[5,6] There is also the belief that a patient who feels well could stop medication.[6] Intensive health education would be required to address these factors especially at diagnosis. It is important to identify social supports for the newly diagnosed that would remind and encourage them to take medicines and to strive for universal health insurance coverage to facilitate access to medicines.

This study has a number of limitations. First, the baseline blood pressure reading at diagnosis and subsequently at follow-up were not available for the majority of cases. As such, only blood pressure reading documented at admission prior to death of the cases was available for this study. Part of the reason for this was that some of the patients were not primarily patients of the University College Hospital, Ibadan and were brought in by the relatives without referral information. Second, most of the patients had poor compliance with their medication which suggests that healthcare-seeking behavior and follow-up visit by patients were poor, educating patients and their relatives of their diseases might help improve such behaviors. The absence of follow-up blood pressure recordings made it difficult to determine what effect antihypertensive therapy had on blood pressure control. Third, the very few cases that reported medication compliance reduce the power of this study to determine the true significance of drug compliance on survival interval. Fourthly, the documentation on treatment compliance was not further explored. This is because records of objective assessment of medications compliance such as daily drug intake charts, appropriate dosage, and time of the day medication was taken were not available. This will enable uniformity of responses and help define what drug compliance means for the population studied which will impact on public health education intervention. Despite these limitations, the outcome of this study is similar to prospective follow-up studies in Nigeria and Britain and might suggest that the mean blood pressure in this study may not differ significantly from the baseline values.[11,12]

CONCLUSION

This study showed a high level of reported systemic hypertension status awareness among individuals dying from hypertension-related complications but very poor compliance with prescribed medication. Noncompliance to medication was associated with worse cardiovascular disease and all-cause mortality outcomes. It is likely that regular medication intake will reduce the cardiovascular events associated with essential hypertension in our environment. Efforts should be intensified by healthcare practitioners and advocates both at the hospital and public settings to sensitize and educate the patients and the public respectively on the need to effectively control blood pressures and mitigate these untoward adverse outcomes.

Conflicts of interest
There are no conflicts of interest.

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