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Hypertension in a resource-limited setting: Poor Outcomes on Short-term Follow-up in an Urban Hospital in Maputo, Mozambique

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Abstract

Mozambique has low levels of detection, treatment, and control of hypertension. However, data on target organ damage and clinical outcomes are lacking. The authors aimed at characterizing the clinical profile, pattern of target organ damage, and short-term outcomes of patients referred to a first referral urban hospital in a low-income setting in Africa. We conducted a prospective descriptive cohort study from February 2016 to May 2017 in Maputo, Mozambique. Adult patients with systolic and diastolic blood pressure ≥180 mm Hg and/or ≥110 mm Hg, respectively, or any systolic blood pressure above 140 mm Hg and/or diastolic blood pressure above 90 mm Hg in the presence of target organ damage (with or without antihypertensive treatment) were submitted to detailed physical examination, funduscopy, laboratory profile, electrocardiography, and echocardiography. Six months after the occurrence of complications (stroke, heart failure, and renal failure), hospital admission and death were assessed. Overall, 116 hypertensive patients were recruited (mean age 57.5 ± 12.8 years old; 111[95.7%] black; 81[70%] female) of which 79 had severe hypertension. The baseline mean values recorded for systolic and diastolic blood pressure were 192.3 ± 23.6 and 104.2 ± 15.2 mm Hg, respectively. Most patients (93; 80.2%) were on antihypertensive treatment. Patients' risk profile revealed dyslipidemia, obesity, and diabetes in 59(54.1%), 48(42.5%), and 23(19.8%), respectively. Target organ damage was found in 111 patients. The commonest being left atrial enlargement 91(84.5%), left ventricular hypertrophy 57(50.4%), hypertensive retinopathy 30(26.3%), and chronic kidney disease 27(23.3%). Major events during 6-month follow-up were hospitalizations in 10.3% and death in 8.6% of the patients. Worsening of target organ damage occurred in 10 patients: four stroke, two heart failure, and four renal damage. Patients with severe hypertension and target organ damage were young with high-risk profile, low hypertension control, and high occurrence of complications during short-term follow-up. Efforts to improve high blood pressure control are needed to reduce premature mortality in this highly endemic poor setting.

1 | INTRODUCTION

Hypertension (HTN) is a global health problem, with high prevalence worldwide.[1,2] It is a well-known risk factor for ischemic heart disease, congestive heart disease, diastolic dysfunction, and stroke and is commonly associated with left ventricular hypertrophy (LVH), proteinuria and kidney failure, retinopathy, and vascular dementia, which fall under the concept of "target organ damage" (TOD).[3] HTN severity is a strong determinant for TOD,[4] especially in African descent.[5,6]

In Mozambique, despite the rise in HTN prevalence from 33.1% in 2005 to 38.9% in 2015, there are low rates of awareness, many are untreated or poorly treated, and few are controlled.[7,8] HTN is a major reason for demand for health care,[9] but there are no studies on the burden of TOD in hypertensive Mozambicans attending health facilities. To address this lack of knowledge on profile of complications and clinical outcomes, we designed a study aiming at characterizing severe and complicated HTN, as well as determining clinical outcomes in a resource-limited environment.

2 | METHODS

We designed a prospective descriptive cohort study to assess adult patients with hypertension referred from outpatient clinic and hospital wards to specialist care, presenting with systolic blood pressure (SBP) ≥180 mm Hg and/or diastolic blood pressure (DBP) ≥110 mm Hg or any SBP values above 140 mm Hg and/or DBP values above 90 mm Hg in the presence of TOD, with or without antihypertensive treatment. We included patients with left atrial enlargement (LAE), LVH, proteinuria or chronic kidney disease (CKD), hypertensive retinopathy, and stroke. Pregnant women and those living outside Maputo city were excluded from the study. The study was conducted from February 2016 to May 2017 at Mavalane General Hospital in Maputo-Mozambique.

A structured questionnaire was used to collect socio-demographic data from all patients including date of birth, sex, race, occupation, school level, and marital status. Regarding the level of education obtained, participants were classified as "Primary" when they had completed 7 years of education or less; "Secondary" when they had completed secondary school, meaning in total 12 years of education; and, finally, "Tertiary" when they had obtained a university or professional degree. We also collect data on past personal medical history (previous diagnose of HTN, diabetes mellitus, stroke, and heart disease), the pattern of physical activity, alcohol consumption, and smoking habits. Self-reported use of antihypertensive medication or any other drugs was registered.

Patients were submitted to physical examination, laboratory profile, electrocardiography, and transthoracic echocardiography.

2.1 | Physical examination

Anthropometric measurements (weight, height, and waist circumference) were performed using standardized methods. Trained health workers obtained blood pressure (BP) according to International Society of Hypertension guidelines, using a validated automatic sphygmomanometer (OMRON M2 Plus; OMRON Healthcare, Kyoto, Japan) and appropriately sized cuff. BP was measured in both arms in sitting position and repeated after 5 minutes' rest; for analysis, we used the mean of the two measurements from the right arm.

Hypertension was defined as SBP values ≥130 mm Hg and/or DBP values ≥90 mm Hg.[10] Severe HTN was defined as SBP values ≥180 mm Hg and/or DBP ≥110 mm Hg or SBP ≥160 mm Hg and DBP values ≥100 mm Hg in the presence of TOD—impairment in the function of a target organ such as the brain, arteries, heart, eyes, and kidney,[11] with or without antihypertensive treatment, and complicated hypertension was defined as values of SBP above 140 mm Hg and/or DBP above 90 mm Hg in the presence of TOD,[11] with or without antihypertensive treatment. Controlled HTN was defined by values of SBP <130 mm Hg and DBP <90 mm Hg in patients using antihypertensive medication; the average on the follow-up visits was used as a criterion for the diagnosis of controlled BP at six months.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared [weight (kg)/height (m^2)] and categorized as per the World Health Organization guidelines (WHO), namely underweight (BMI < 18.5 kg/m^2), normal (BMI ≥ 18.5 to ≤24.9 kg/m^2), overweight (BMI ≥ 25.0 to ≤29.9 kg/m^2), or obese (BMI ≥ 30.0 kg/m^2).[12] Waist circumference was used as a measure of abdominal obesity; measurements were done to the nearest 0.1 cm, using a constant tension tape, directly over the skin, at the level of the midpoint between the inferior margin of the last rib and the iliac crest in the mid-axillary line in all patients. For analysis, the cutoffs used were waist circumference ≥102 cm in men and ≥88 cm in women.[13] Measurements were done with the participant dressed in light clothing and without shoes.

Hypertensive heart disease (HHD) was diagnosed according to the European Society of Cardiology guidelines[14,15] (left ventricular fractional shortening below 25% and left atrial enlargement; or clinically by the presence of signs of congestive heart disease such as increased pressure of jugular veins, 3rd heart sound, congestive hepatomegaly, and peripheral edema).

Stroke was defined as "a focal (or at times global) neurological impairment of sudden onset, lasting more than 24 hours (or leading to death), and of presumed vascular origin," as per World Health Organization clinical definition[16]; it was also identified through the history of a previous event (including transient ischemic stroke) and a focused neurological examination looking for motor or sensorial defects.

An experienced ophthalmologist blinded to the BP levels carried out the funduscopic retinal examination. Hypertensive eye damage was diagnosed based on the Keith-Wagner-Barker criteria for hypertensive retinopathy; patients were divided into 4 grades according to the presence of retinal arteries narrowing, sclerosis, and tortuosity of the retinal arterioles.[17]

2.2 | Laboratory profile

Venous blood was collected from all patients for biochemical assessment including the levels of fasting blood sugar (FBS), total cholesterol, triglycerides (TG), urea, creatinine, uric acid, albumin, full blood count, and human immunodeficiency virus (HIV) infection status. Hyperglycemia was defined as fasting plasma glucose 5.6-6.9 mmol/L and diabetes mellitus (newly-diagnosed) as fasting plasma glucose of 7.1 mmol/L or above.[17] Hypertriglyceridemia was defined as TG greater than 1.7 mmol/L,[18] and dyslipidemia was defined as total cholesterol ratio more than 5.2 mmol/L.[18,19] Anemia was defined as hemoglobin levels below 12 mmol/L for non-pregnant women and 13 mmol/L for men.[20]

Chronic kidney disease (CKD) was defined by a confirmed positive dipstick proteinuria, albuminuria (at least traces), and/or estimated glomerular filtration rate (eGFR) < 90 mL/min/1.73 m^2.[21] The Kidney Disease Improving Global Outcomes (K/DIGO) guidelines were used to stage participants for GFR categories and albuminuria categories of CKD.[21] The eGFR categories included grade 1 (eGFR ≥ 90), grade 2 (eGFR 60-89), grade 3 (eGFR 30-59), grade 4 (eGFR 15-29), and grade 5 (eGFR < 15). The GFR (assessed by creatinine clearance) was calculated using the CKD-EPI Creatinine 2009 Equation [22] Impaired eGFR was defined as an eGFR < 60 mL/min/1.73 m^2. The albuminuria categories of CKD were as follows: P1 (negative), P2 (trace to 1+ [30 mg/dL]), P3 (30-300 mg/dL), and P4 (>300 mg/dL).[23]

2.3 | Cardiac evaluation

A 12-lead electrocardiogram (ECG) and focused transthoracic echocardiography were performed. LVH on ECG was based on Sokolow-Lyon criteria.[24] Under the focused cardiac ultrasound protocol, left atrial to initial aorta ratio and shortening fraction were calculated, according to the American Society of Echocardiography,[25,26] while left ventricular (LV) ejection fraction was visually assessed. Hypertensive cardiac damage was defined by fractional shortening below 25% and left atrial enlargement (LAE) by a left atrium bigger than the aorta diameter.[26] Aortic enlargement was defined as aortic root dimension above 40 cm.[26]

2.4 | Follow-up

At 6 months, we assessed the occurrence of complications such as hypertensive heart disease, stroke, renal failure, hospital admission, and death.

2.5 | Statistical analysis

Data were entered into an Excel database and analyzed using SPSS *software* version 20.0 (SPSS Inc, Chicago, Illinois, USA). Descriptive analysis of the variables was performed to process the data as tables (cross-tabulations). Normal distributed continuous variables are represented as the means and standard deviation (SD) and non-Gaussian distributed variables as the median. Categorical variables were described using frequency tables (percentages). The independent Student's *t* test was used for continuous variables, and chi-square tests were used to assess significance. Discrete variables were analyzed via odds ratios with 95% confidence intervals. *P*-value < .05 was considered statistically significant.

2.6 | Ethics approval and consent to participate

The study was approved by the National Bioethics Committee for Health of Mozambique with reference number 38/CNBS/16. Written informed consent was obtained from all patients.

3 | RESULTS

We invited 120 patients of these 116 were included; four were excluded because two have moved out of Maputo Province and two withdrawn the informed consent for personal reasons. Two-third of the patients were less than 65 years old (around 15% younger than 44 years), over 80% had limited formal education, and 65% had no fixed payday. The baseline socio-demographic characteristics of patients are shown in Table 1.

3.1 | Risk profile

Of the 116 patients (81 women, 70%; mean age 58 years; 18 (15.5%) below 45 years) enrolled, 79 were recruited with severe HTN and only five patients did not present TOD. Self-reported established cardiovascular disease was found in 45 patients (38.8%); 23 (19.8%) patients had previous or present stroke or transient ischemic attack, and 22 (18.9%) had a previous/present signs of congestive heart disease. The frequency of self-reported diabetes mellitus was 8.6%, and the frequency of other cardiovascular risk factors was as follows: smoking habits 6.9% (all men), alcohol consumption 47.4%, and physical inactivity 93.9% patients (Figure 1). Over ¾ of the patients (83 of 113) were overweight (BMI ≥ 25 kg/m^2), of which 48 (42.5%) were obese (BMI ≥ 30 Kg/m^2). Three patients were unable to stand due to the sequela of stroke and were classified using abdominal circumference. Abdominal obesity was present in 72 (53.4%) patients (13 of 34 men vs 59 of 81 women) (Table 2).

At baseline, 93 of 116 (80.2%) patients reported being on antihypertensive drugs for at least three months preceding entry in the study; none had the BP controlled (< 130/90 mm Hg). The antihypertensive drugs used (either alone or in combination) included thiazide diuretics in 91(97.8%) patients, calcium channel blockers in 40 (43%), angiotensin-converting enzyme inhibitors in 34 (36.6%), and beta-blockers in 7 (7.5%). The mean SBP and DBP values did not vary according to the sex SBP 191.4 (SD ± 22.3) mm Hg/DBP 104.1 (SD ± 15.5) mm Hg in men versus SBP 192.7 (SD ± 24.3) mm Hg/DBP 104.3 (SD ± 15.2) mm Hg (*P* = .82 vs *P* = .93) in women.

TABLE 1 Socio-demographic data of 116 patients

	Total (n = 116)	Males (n = 35)	Females (n = 81)
Age			
Mean age ± SD	57.5 ± 12.8	58.7 ± 13.3	56.98 ± 12.7
Median age. Years	58	61	57
18-44 years	18 (15.5)	6 (17.1%)	12 (14%)
45-64 years	62 (53.4%)	17 (48.6%)	45 (55.6%)
≥65 years	36 (31.0%)	12 (34.3%)	24 (29.6%)
Race			
Black	111 (95.7%)	33 (94.3%)	78 (96.3%)
Asian	5 (4.3%)	2 (5.7%)	3 (3.7%)
Level of education			
None	20 (17.2%)	1 (2.9%)	19 (23.5%)
Primary	73 (62.9%)	22 (62.9%)	51 (63.0%)
Secondary	19 (16.4%)	9 (25.7%)	10 (12.3%)
Higher	4 (3.4%)	3 (8.6%)	1 (1.2%)
Status marital			
Single	9 (7.8%)	3 (8.6%)	6 (7.4%)
Married	69 (59.5%)	29 (82.9%)	40 (49.4%)
Divorced	7 (6.0%)	1 (2.9%)	6 (7.4%)
Widower	31 (27.7%)	2 (5.7%)	29 (35.8%)
Occupation			
Jobless	54 (46.6%)	3 (8.6%)	51 (63.0%)
Traders	21 (18.1%)	4 (11.4%)	17 (21.0%)
Pensioners	7 (6.0%)	7 (22.6%)	0
Others	33 (28.4%)	20 (57.1%)	13 (16.0%)

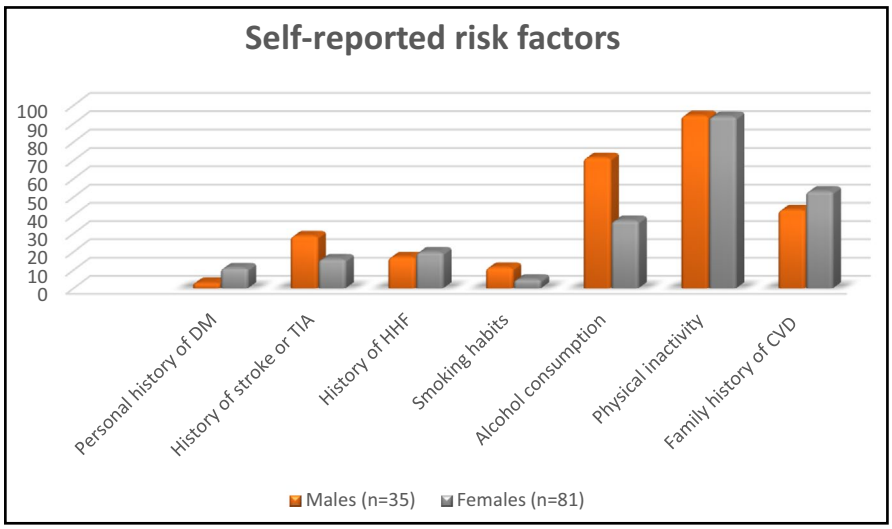

FIGURE 1 Self-reported risk factors groups in male (n = 35) and female (n = 81). CVD, cardiovascular disease; DM, diabetes mellitus; HF, heart failure; TIA, transient ischemic attack

Fifty-nine out of 109 (54%) had dyslipidemia, 28 out of 110 (25.5%) had hypertriglyceridemia, and 23 out of 116 (20%) had diabetes mellitus. Over one-quarter of all patients (31; 27%) had anemia that was higher in women when compared to men (30 vs 1; $P < .001$). Nineteen percent (22 of 116 patients) were HIV infected; of those, 21 had been receiving antiretroviral therapy (Table 2).

3.2 | Target organ damage

The profile of TOD is shown in Table 3. The organs most frequently damaged were the heart and kidney. Among the 103 patients submitted to transthoracic echocardiography, left atrial enlargement (LAE) was found in 91 (84.5%), of which 9 had atrial fibrillation; LVH

TABLE 2 Biological profile of the patients enrolled in the study

	Total	Males	Females	*P*-value
Mean SBP (mm Hg)	192.4 (±23.6)	191 (±22.3)	192.7 (±24.3)	.827
Mean DBP (mm Hg)	104.2 (±15.2)	104.1 (±16)	104.3 ± 15.2	.932
Mean BMI kg/m^2; N:113	28.9 (±5.9)	28.3 (±5.1)	29.1 (±6.2)	.479
BM 25-29.9 Kg/m^2	35 (31%)	13 (38.2%)	22 (27.8%)	.273
BMI ≥ 30 kg/m^2	48 (42.5%)	12 (38.2%)	36 (45.6%)	.311
Mean WC; N:115	97.1 (±15.0)	99.3 (±14.6)	96.2 (±15.2)	.507
WC	-	M: ≥102 cm	W: ≥ 88 cm	
		13/34 (39.5)	59/81 (72.8)	
Mean TG (mg/dL) N: 110	1.51 (±1.1)	1.4 (±0.8)	1.6 (±1.2)	.507
TG > 1.7 mg/dL	28 (25.5%)	7 (20.6%)	21 (27.6%)	.433
Mean cholest (mmol/L) N:109	5.6 (±1.5)	5.3 (±1.2)	5.7 (±1.6)	.198
Cholest > 5.2 mmol/L	59 (54.1%)	15 (45.5%)	44 (57.9%)	.231
Mean FBS N:116	6.1 (±2.1)	5.9 (±1.7)	6.1 (±2.3)	.714
FBS ≥ 7.0 mmol/L	23 (19.8%)	7 (20%)	16 (19.8%)	.976
Mean eGFR (mL/min/1.73 m^2)	79.7 ± 33.8	73.8 ± 24.4	82.3 ± 37.0	.217
Mean Serum uric acid (mg/dL); N:114	387 (±120.8)	421 (±97.8)	371 (±127.2)	**.025**
HGB < 12 mmol/L N:116	31 (26.7%)	1 (2.9%)	30 (37%)	**<.001**
HIV positivity N:116	22 (19%)	5 (14.3%)	17 (21%)	.291
Mean CD4 (cells/mm^3) N: 20	620.8 (±579)	557 (±326)	642 (±649)	.785

Note: Significant *P* values (<.05) in bold.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; HGB, hemoglobin; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.

was present in 57 (50.4%) and LV systolic dysfunction in 19 (18.4%). Renal damage occurred in 27 (23.3%) patients and severe CKD in 10 (8.6%). Grade III hypertensive retinopathy was diagnosed in 15 out of 114 patients submitted to funduscopy. Among patients studied, 44 had one TOD; 44 had two different TOD; 22 had three TOD; and 5 had four TOD. Only five patients did not have any type of TOD.

3.3 | Follow-up at 6 months

Overall among the 116, four patients could not submit to full follow-up as they have moved out of Maputo Province, they were assessed by a phone call and they were in good health. However, information on their vital status and hospitalization was obtained. There were 12 (10.3%) hospitalizations and 10 deaths (8.6%). Of these, one had a stroke, one had a congestive heart disease/pulmonary edema, one was post-surgery, and in seven patients, the cause could not be identified as they died at home. The causes of hospitalization were as follows: 7 had HHD/hypertensive urgency (2 were in congestive heart disease), 1 stroke, 2 had been submitted for a surgery, 1 injury, and 1 malaria. De novo strokes, HHD, and renal failure occurred in four, two, and four patients, respectively (Table 4).

The mean number of visits per patient over the follow-up period was four. The most used drugs were thiazides diuretics (hydrochlorothiazide with an amiloride), followed by calcium channel blockers (nifedipine and amlodipine) and angiotensin-converting enzyme inhibitors (enalapril). Only 25.3% had SBP controlled at 6 months. The mean values of BP on 6-month follow-up were SBP 151 (SD ± 26.6) and DBP 82.9 (SD ± 12.7) mm Hg; the mean reduction was 41.4 mm Hg for SBP and 21.3 mm Hg for DBP (Table 5).

4 | DISCUSSION

This hospital cohort revealed high-risk profile, high levels of BP, low control rates, and poor outcomes on short-term follow-up of relatively young people from an urban setting, referred to a first referral hospital in a low-income country. Over 2/3 of the patients were less than 65 years old (around 15% younger than 44 years), over 80% had limited formal education, and 65% had no fixed payday. There were high levels of obesity (42.5%), type 2 diabetes (19%), dyslipidemia (over 50%), HIV infection (20%), and anemia (30%). The low socioeconomic profile and concerning pattern of multimorbidity in hypertensive patients were associated with high occurrence of established and/or de novo target organ damage, as well as high hospitalization and case-fatality rates on short-term follow-up.

In our urban cohort, the frequency of overweight/obesity was higher than that obtained from the two last WHO STEPS survey in the general population countrywide.[7,8,27] Obesity was predominant in female sex in line with other studies in the continent.[27-29] Type 2

TABLE 3 Frequency of TOD in 116 patients enrolled in the study at baseline

Target organ damage	Number	Prevalence (%)
LVH	57/113	50.4
LAE	91/103	84.5
Atrial Fibrillation	9/113	8.0
Systolic dysfunction	19/103	18.4
Hypertensive Retinopathy	30/114	26.3
Grade 0	84/114	73.7
Grade 1	1/114	0.9
Grade 2	14/114	12.3
Grade 3	15/114	13.2
Grade 4	0/114	0.0
Albuminuria	29/113	25.7
Negative	84/113	74.3
Trace albuminuria (15-30 mg/dL)	10/113	8.8
P2-P3 albuminuria (30 - 300 mg/dL)	17/113	15.0
P4 albuminuria (>300 mg/dL)	2/113	1.8
CKD (K/DIGO CKD stage)	27/116	23.3
Stage 1 eGFR ≥ 90	42/116	36.2
Stage 2 eGFR 60-89	47/116	40.5
Stage 3 eGFR 30-59	17/116	14.7
Stage 4 eGFR 15-29	5/116	4.3
Stage 5 eGFR < 15	5/116	4.3

Abbreviations: CKD, Chronic Kidney Disease; eGFR, Estimated Glomerular Filtration Rate; LAE, Left Atrial Enlargement; LVH, Left Ventricular Hypertrophy.

diabetes mellitus (19%) and dyslipidemia (50%) were both above the frequency reported in the general population in Mozambique[27,30] and other regions.[4,31,32] While rapid urbanization is associated with behavioral changes that increase the risk of chronic non-communicable diseases,[33] the socioeconomic characteristics of our population show a mixed risk of behavioral and poverty-related determinants, that may at least partially explain the low rate of blood pressure control and the high occurrence of TOD such as heart failure and stroke, known to be common in our setting.[30,34]

Almost two-thirds of the patients (64.7%) had no fixed payday (46.6% were unemployed and 18.1% traders), an expected finding in peri-urban settings of low-income countries such as Mozambique. Low and erratic family income may have determined the mode of presentation of these patients, which had advanced disease and several complications. In concordance with other countries in the SSA (Sub-Saharan Africa) region, Mozambique has a low percentage of people with health insurance, related to the high rates of unemployment.[4,35] Low insurance rates may have contributed to lower treatment coverage and BP control in this study population, as shown by other authors.[35-38] Other factors that may have contributed for presentation with severe disease are the high proportion of patients living without a partner (single/separated and widows) and the high percentage of illiteracy (only 19.9% had the primary level completed). High adult illiteracy rates have been reported in developing countries.[4,36] Although no questions regarding income were asked, illiteracy, loneliness, and poverty are known determinants of uncontrolled BP, by leading to poor adherence to hypertensive treatment, stress, and depression, especially in elderly patients.[36,39,40] For instance, the low level of education of the overall study population surely influences the understanding of the importance of adequate and regular medication, an issue that needs to be taken into account when designing health education strategies and policies.

Despite the high rate of self-reported treatment at entry to the study, the mean SBP levels and DBP at baseline were higher—with no difference between men and women—than those obtained in Nigeria and Cameron.[4,28,41] At six-month follow-up, there was still a considerable proportion of patients with uncontrolled blood pressure and the mean levels had not reach normal values, and several adverse events had occurred including de novo TOD, hospitalizations, and deaths. These results show the urgency for tailored approaches to implementing evidence-based strategies for earlier diagnosis and improved referral systems and preventive measures for this high-risk population.

The present study suggests that, like in similar settings in SSA,[4,28,42] hypertension is an important cause of premature disability and death in our cohort. This poor prognosis in our cohort is partially driven by the high occurrence of several conventional risk factors for cardiovascular disease concomitantly, namely obesity, dyslipidemia, and diabetes, but also due to the high prevalence of anemia (33%) and HIV infection (19%). This multimorbidity pattern in predominantly illiterate people assisted in a high demand and under-resourced health service that does not allow enough time and resources for health education also predisposes to poor outcomes. Multimorbidity is associated with higher levels of health care utilization and greater financial burden for individuals in middle-income countries, imposing an unbearable economic burden on the health care system,[43] and increasing the risk of catastrophic spending in health.

Severe hypertension and HIV infection constitute major drivers of cardiovascular risk in SSA region.[30,34,44] Mozambique suffers one of the SSA highest burdens of HIV and acquired immunodeficiency syndrome (AIDS) with prevalence around 13.2% in adults,[45] and since 2004 started expanding the use of highly active antiretroviral therapy,[46] and more recently adopted the *"Prevent HIV, Test and Treat all"* strategy, where all patients tested positive for HIV should be initiated ARVs (antiretroviral) therapy regardless of the CD4 value according to WHO guidelines.[47] In our cohort, the frequency of HIV infection (19%) was also higher than that reported in general population in 2015.[45] HIV infection predisposes to premature atherosclerosis through endothelial dysfunction, pro-inflammatory state, and dyslipidemia,[48] and higher risk of cardiovascular and metabolic complications is expected with longer ARV therapy.[49]

The TOD pattern is similar to that found in similar settings in Africa, but is highly concerning due to the low age of our population.

TABLE 4 Characterization of severe and complicated hypertension, HIV infection, and mortality and survival group

	Severe HTN group N = 79	Complicathtn group N = 38	HIV positive group N = 22	HIV negative group N = 94	Mortalit group N = 10	Survival group N = 106
Median Age N:116	56,23	60,08	58,81	51,86	60,50	57,21
Mean SBP N:116	203,03	169,55	193,18	191.80	187,2	192,52
Mean DBP N;116	109,35	93,74	103,49	107,41	106,4	104,04
BMI ≥ 30 kg/m^2 N:113	36 (45.6%)	12 (31.6%)	3 (13.6%)	45 (47.9%)	2 (20%)	46 (43.4%)
Cholest > 5.2 mmol/L N:109	31 (39.2%)	28 (73.7%)	8 (36.4%)	51 (54.2%)	5 (50%)	54 (50.9%)
FBS ≥ 7 mmol/L N:116	13 (16.4%)	10 (26.3%)	1 (4.5%)	22 (23.4%)	2 (20%)	21 (19.8%)
HIV Positivity N:116	16 (20.2%)	6 (15.8%)	-	-	2 (20%)	8 (7.5%)
CKD N:116	15 (19%)	12 (31.6%)	6 (27.2%)	21 (22.3%)	5 (50%)	22 (20.8%)
LVH N:113	40 (50.6%)	17 (44.7%)	14 (63.6%)	43 (45.7%)	4 (40%)	53 (50%)
Hypertensive retinopathy N:114	19 (24.1%)	11 (28.9%)	1 (4.5%)	3 (3.2%)	1 (10%)	29 (27.4%)
OUTCOMES						
Stroke[a] N:116	3 (3.8%)	1 (2.6%)	1 (4.5%)	3 (3.2%)	2 (20%)	2 (20%)
Renal failure[a] N:95	4 (5.1%)	1 (2.6%)	1 (4.5%)	4 (4.2%)	1 (10%)	4 (3.8%)
Congestion HD[a] N:116	2 (2.5%)	0 (0%)	1 (4.5%)	1 (1.1%)	2 (20%)	0 (0%)
Hospitalizations N:116	4 (5.1%)	8 (21.1%)	1 (4.5%)	11 (11.7%)	3 (30%)	9 (8.5%)
Death N:116	6 (7.6%)	4 (10.5%)	3 (13.6%)	7 (7.4%)	-	-

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; DBP, diastolic blood pressure; FBS, fasting blood sugar; HTN, hypertension; HD, heart disease; LVH, left ventricular hypertrophy; SBP, systolic blood pressure.

[a]New event during the 6-month follow-up.

Only five patients did not have TOD, and a high proportion had multiple organs affected (>3 organs in damage in 27%). Heart damage was the main driver of TOD, followed by hypertensive retinopathy and kidney damage. Cardiovascular complications were common, the most frequent abnormalities being LAE (84%), LV systolic dysfunction (50%), stroke (20%), and atrial fibrillation (8%). Additionally, around 25% had severe renal damage (GFR below than 60 mL/min and/or albuminuria) and the same percentage had hypertensive retinopathy: two patients *had these two abnormalities together.* Some type of TOD was found in 111 out of 116 hypertensive adults at diagnosis and over short follow-up, corroborating reports from Nigeria[4,28] and Ghana.[42]

We found a high frequency of LVH, which is known to increase the risk of stroke or cerebrovascular disease, coronary heart disease, and HF and cardiac mortality.[50,51] Left atrial enlargement has also adverse prognostic implications in hypertension, namely as an independent predictor of atrial fibrillation,[52] thrombo-embolic stroke,[53] congestive heart disease, and cardiovascular death.[54,55] Additionally, cross-sectional analyses conducted in patients with non-valve atrial fibrillation concluded that the extent of left atrial dilatation is related to the severity of ischemic stroke.[55]

The most common cause of end-stage renal failure in younger individuals in SSA is hypertension.[43,56] In our cohort, albuminuria was present in one-quarter of the patients, using dipstick albuminuria method confirming their vulnerability to hypertensive kidney disease and risk of chronic renal failure.[57] The frequency of microalbuminuria (15.0%) was higher than that reported in Nigeria (12.3%)[28] but lower than values found in Zambia (26.9%),[58] in Nigeria (32.3% and 37%),[59,60] and in Cameroon (39.3%),[41] as well as in studies done in North America (21.6%) and Europe (16.8%).[61] The occurrence of macroalbuminuria (1.8%) was similar to that found in Nigeria (2.0%),[60] while much higher values reported from Zambia, Ghana, and Nigeria, respectively, at 8.9%,[58] 13.4%,[42] and 15.2%.[28] The frequency of impaired eGRF was also higher compared to some similar studies in SSA region,[4,62] as well as America and Europe.[61]

TABLE 5 Comparison of BP controls and risk factors between baseline and follow-up of patients enrolled in the study

	At baseline	After 6 months
Mean SBP Control N:102	192.4 ± 23.6	151 ± 26.6
Mean DBP Control N:102	104.2 ± 15.2	82.9 ± 12.7
SBP < 130 mm Hg N:102	0 (0%)	25 (25.3%)
DBP < 90 mm Hg N:102	19 (16.4%)	67 (67.7%)
BMI ≥ 30 kg/m^2 N:98	48 (42.5%)	35 (35.7%)
eGFR < 60 mil/min per 1,73 m^2 N:95	27 (23.2%)	15 (15.8%)
Cholesterol > 4.9 mmol/L N:97	69 (63.3%)	55 (57.6%)
TG > 1.7 mg/dL N:95	28 (25.5%)	19 (20%)
FBS ≥ 7.0 N:95	23 (19.8%)	9 (9.5%)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBS, fasting blood sugar; SBP, systolic blood pressure; TG, triglycerides.

Over the 6-month follow-up, the occurrence of stroke, heart failure, and impaired GFR was elevated. The high numbers of patients with uncontrolled HTN, diabetes mellitus, obesity, dyslipidemia, HIV infection, LVH, and LAE may explain the high incidence of stroke and its high in-hospital case fatality. [53,63,64] A high incidence of stroke is known to occur in the Mozambican population.[30] Finally, high frequency of hospitalizations and deaths was found in our cohort in short-term follow-up, indicating the aggressive nature of HTN in our study population.

This study highlights the fact that simple, non-invasive, and increasingly accessible techniques (funduscopy, ECG, and abbreviated ultrasound) can be used as tools for risk stratification of patients referred to hospitals in underserved settings. For instance, one-quarter of patients had hypertensive retinopathy, with frequency of grade 3 hypertensive retinopathy being higher than that found in similar populations in Africa.[28,42,60] These high-risk individuals are often neglected in our setting since funduscopy is not usually performed by front line health providers. ECG can also be used as a first-line marker for detection of subclinical cardiac damage in hypertensive patients. Finally, abbreviated ultrasound performed by non-cardiologists may also help in assessing and managing HTN patients presenting with complications; this imaging method has become more available in Mozambique, but it is still restricted to a small number of referral centers of urban areas or to some tertiary centers in rural areas due to its costs and to the lack of expertise to perform the examinations.[65,66]

As low- and middle-income countries populations are aging, the prevalence of multimorbidity (more than two co-existing chronic conditions) is expected to significantly increase the pressure on already stretched health systems. Patients with diabetes, stroke, and depression had the largest effect on increasing mean number of outpatient visits, increasing mean number of hospitalization days. The health systems in these under-resourced settings should consider the needs of patients with different multimorbidity patterns to effectively respond to the demands on health care utilization[67] Health care systems must adapt by working toward integrated primary care for HIV/AIDS and non-communicable diseases[68,69] and other infections such as tuberculosis and malaria which cause chronic sequelae like chronic obstructive pulmonary disease and anemia, respectively.

4.1 | Limitations

The results we here present derive from a small population of patients seen at a single center for a short follow-up and therefore are not representative or generalizable of the whole population. Another limitation to consider is the fact that we could not get verbal autopsies for the patients who died out of the hospital. Nevertheless, our results clearly unveil concerning risk profile, low HTN control rates, high TOD incidence, and poor outcomes over a short follow-up. Moreover, they describe socioeconomic determinants that contribute to multimorbidity that should guide policy making, health education, and organization of hospital services in low-income settings facing the new challenges linked to providing care to address non-communicable diseases.

5 | CONCLUSION

Severe and complicated HTN presenting in young adults with high-risk profile and multimorbidity determined high case-fatality and hospitalization rates on short-term follow-up. Active screening and prompt management of HTN at primary care level is needed, using context-specific algorithms that take into account the health determinants and the conditions of the health system. These results suggest that in resource-limited setting in addition to risk stratification of patients, innovative and efficient use of resources and investment on early prevention will be required to reduce premature mortality caused by HTN.

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COMPETING INTEREST

The authors declare that they have no competing interests.

AUTHOR'S CONTRIBUTIONS

NM and AM conceived and designed the study; NM, RM, JD, and AM performed the procedures. NM, KS, and AM analyzed and interpreted data. NM drafted the manuscript. KS, SL, and AM critically reviewed for important intellectual content of the manuscript versions. All authors approved the final manuscript.

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