



Published in final edited form as:

J Hum Hypertens. 2022 February ; 36(2): 144–152. doi:10.1038/s41371-020-00464-6.

24-hour ambulatory blood pressure monitoring and hypertension related risk among HIV-positive and HIV-negative individuals: Cross sectional study findings from rural Uganda.

Anxious J. Niwaha^{1,2,3}, Adaeze C. Wosu^{2,4}, Christabellah Namugenyi⁵, Alex Kayongo^{2,6}, Moffat J Nyirenda³, Trishul Siddharthan^{2,7}, William Checkley^{2,7}, Fred C. Semitala^{1,6}, Robert Kalyesubula^{3,6,8}

¹Makerere University Joint AIDS Program (MJAP), Makerere University College of Health Sciences, Kampala Uganda

²Center for Global Non-Communicable Disease Research and Training, School of Medicine, Johns Hopkins University, Baltimore, Maryland, USA

³Non-Communicable Diseases (NCD) Theme, MRC/UVRI and LSHTM Uganda Research Unit, Entebbe Uganda

⁴Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

⁵School of Statistics and Planning, Makerere University, Kampala, Uganda.

⁶Department of Medicine, College of Health Sciences, Makerere University, Kampala Uganda

⁷Division of Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland, USA

⁸African Community Center for Social Sustainability (ACCESS), Nakaseke, Uganda

Abstract

Hypertension is diagnosed and treated based on blood pressure (BP) readings obtained in the clinic setting. Positive HIV status is associated with a higher prevalence of abnormal diurnal blood pressure patterns, diagnosed with ambulatory BP monitoring rather than the conventional method of BP measurement. Little is known about ambulatory BP profiles in people living with HIV (PLHIV) in low-income countries, especially within sub-Saharan Africa. In this study,

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Correspondence should be addressed to: Anxious J Niwaha, MB.Ch.B, Non-Communicable Diseases (NCD) Theme, Medical Research Council/ Uganda Virus Research Council and London School of Hygiene and Tropical Medicine, Research Unit, Entebbe, Uganda (Anxious.Niwaha@mrcuganda.org).

Authors' contribution

Conception and design, A.J.N., T.S., A.K., F.C.S., R.K., and W.C. Analysis and interpretation, A.J.N., A.C.W., C.N., T.S., M.J.N., F.C.S., R.K., and W.C. Drafting the manuscript for important intellectual content, A.J.N., A.C.W., T.S., M.J.N., F.C.S., R.K., and W.C.

Data availability

The data underlying the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of interest

The authors declare no conflict of interest regarding the publication of this paper.

we compared 24-hour ambulatory blood pressure profiles of 140 HIV-positive individuals vs. profiles in 166 HIV negative individuals living in rural Uganda. HIV was well-controlled, with all HIV seropositive participants reporting use of anti-retroviral therapy, and approximately 123 (88%) having undetectable viral load. Most participants reported ART use duration of less than 10 years. Compared to HIV negative participants, HIV positive participants had lower median 24-hour systolic blood pressure (110.4 mmHg (IQR: 105.7, 118.7) vs 117.7 mmHg (IQR: 110.8, 129.8), $p < 0.001$), and 24-hour diastolic blood pressure (69.2 mmHg (IQR: 65.0, 74.9) vs. 71.9 mmHg (IQR: 67.2, 78.1), $p = 0.004$). Adjusted results showed greater percentage systolic nocturnal dipping among PLHIV compared to HIV negative individuals (difference = 2.70 (IQR: 0.94, 4.47), $p < 0.05$). Results of the adjusted Poisson regression suggested lower prevalence of 24-hour and night hypertension among HIV positives compared to HIV negative, but were not statistically significant. Our data suggest that continuous 24-hour blood pressure measurements are lower in PLHIV on ART compared to HIV negative individuals.

Introduction

Increased availability and accessibility of antiretroviral therapy (ART) has led to successful HIV control in sub-Saharan Africa (1). Among people living with HIV (PLHIV) in SSA, more than 70% had access to ART, and of which, 87% were virally suppressed (2). PLHIV now have increased longevity and are more likely to develop cardiovascular diseases (CVDs) compared to the general population (3–6). The potential mechanisms for the increased CVD risk among PLHIV include high prevalence of traditional CVD risk factors like high blood pressure (hypertension), smoking and dyslipidaemia (7), cumulative exposure to ART leading to metabolic derangements (side effects) (8, 9), as well as continuing low grade chronic inflammation and immune activation even with adequate viral suppression (7). The long-term clinical outcomes of PLHIV are therefore increasingly dependent on early identification and management of a range of risk factors for CVD complications (10, 11). However, this has not been given ample attention (12), particularly in sub-Saharan Africa.

Hypertension is the most important risk factor for CVD mortality, and is a growing problem in sub-Saharan Africa (13). The increasing prevalence of hypertension has been reported in both general population (13) and PLHIV in Uganda and other countries in sub-Saharan Africa (14, 15). There are mixed results from previous studies on the burden of hypertension among PLHIV, with a number of studies reporting increased prevalence of hypertension among PLHIV compared to the general population (16, 17). More recent studies among virally suppressed populations have reported a lower prevalence of hypertension in PLHIV than in HIV negative individuals. (18–20).

In most countries in sub-Saharan Africa, hypertension is diagnosed and treated based on BP measurements obtained in the clinic setting. This conventional method provides only a one-time assessment of BP and is affected by various environmental and psychosocial factors, and may therefore not necessarily reflect BP in day-to-day living (21). Single clinic measurements can lead to over-diagnosis (white coat hypertension—i.e., raised BP in the clinic setting and normal BP outside the clinic setting) (22) or under-diagnosis (masked

hypertension—i.e., normal BP in the clinic setting and raised BP outside the clinic setting). Such BP profiles have been reported to be highly prevalent among PLHIV (23). Ambulatory blood pressure monitoring (ABPM) on the other hand provides BP readings taken over the entire 24-hour period in real life scenarios of the individual (24). Ambulatory blood pressure monitoring has also been shown to be a better predictor of CVD risk than more conventional BP measurements, and has been adapted into clinical practice in majority of developed countries(21).

There is however, a scarcity of data on ambulatory blood pressure profiles in PLHIV especially in low-income settings, and in sub-Saharan Africa in particular (23). The limited data available are from small studies (25–27), in selected groups (such as the elderly) (28), or without a HIV negative comparator group (25). We thus sought to determine the 24-hour BP profiles in PLHIV who are ART-treated and HIV negative counterparts in a rural Ugandan population. We also explored factors that are associated with high BP profiles among the two groups.

Materials and Methods

Study design, period and setting

We conducted a cross-sectional study at Nakaseke Hospital between April and September 2018. Nakaseke is a rural district in Central Uganda approximately 66 km north of Kampala. Nakaseke district has seven sub-counties, 49 parishes (323 villages) with an estimated population of 197,369 (29). Nakaseke Hospital is the district hospital with an ART clinic which serves over 2,300 clients, receiving between 50 to 60 clients per day who come from sub-counties within and beyond Nakaseke district.

Participants and sampling

We recruited PLHIV and HIV negative adults living within Nakaseke District. PLHIV were recruited from the ART clinics of Nakaseke District Hospital and Bidabujja Health Centre. These clinics are centrally located within the district and provide comprehensive HIV treatment, care and prevention services. We included patients with HIV positive status, age ≥ 18 years and currently on ART for at least six months, and who had not missed their routine ART visit within the 6 months prior to the study. We excluded women who were pregnant or currently breast feeding, mentally ill patients, those who were not willing to abstain from alcohol use within 24 hours of ambulatory blood pressure monitoring and anyone unable to undergo the study procedures. We also excluded participants who were admitted or critically ill (i.e., unable to carry out normal activity) or working during the night at the time of the study, and HIV negative individuals who did not have documented HIV status results and were not willing to repeat the test. Sampling was based on the order of attendance at the clinic. Health workers at the ART clinics screened patients as they came in for routine HIV services using a screening and eligibility form. Patients who met the eligibility criteria were referred to the study team. After verifying eligibility, we obtained informed consent and allocated a unique identification number to each participant prior to study activities.

HIV negative participants were selected from the surrounding communities of Nakaseke Hospital. Field workers conducted home visits to assess eligibility and referred those who met the inclusion criteria and were willing to take part in the study. Participants were eligible if they tested HIV negative within 3 months prior to the study and were willing to participate in the study. Participants who were willing to take part in the study but had no documented HIV negative results taken at most 3 months prior were first referred for HIV testing services. The health worker (counsellor) screened and referred to the study team each participant from the community that tested negative and met the eligibility criteria in order of attendance. Those who tested HIV positive were enrolled into HIV care and treatment at the ART clinic.

Study procedures and outcome variables

We used a structured questionnaire to record patients' demographic information, environmental risk and anthropometric measurements. We measured height to the nearest centimetre (cm) without shoes and weight measured in light clothing in kilogram (SECA Stadiometer and portable electronic scales, Hamburg, Germany). We calculated Body mass index (BMI) using the formula: $BMI = \text{weight (kg)} / \text{height (m)}^2$. We obtained HIV/AIDS information for HIV positive participants including date of diagnosis, baseline CD4+T cell count, current CD4 count, HIV treatment, HIV RNA level (which is assessed annually for all patients at the clinic) and clinic BP from the patient charts at their respective ART clinics. We recorded information on current anti-hypertensive medication, and other drugs taken by the participant. Trained research nurses uploaded questionnaire data to the server at the end of each day.

24-hour ambulatory blood pressure monitoring

We measured 24-hour BP by fitting participants with a CE/ISO approved 24-hour ABPM monitor [Contec Medical Systems Co., Ltd, Qinhuangdao, China] oscillometric device with an appropriate cuff for mid-upper arm circumference (small, 20–24 cm; medium, 24–32 cm; large, 32–38 cm). The 24-hour ambulatory blood pressure monitors were fitted on a regular working day (i.e., a day during which participants would be undertaking their regular daily activities). Blood pressure was automatically measured at 20-min intervals during the daytime (07:00h – 22:00h) and 30-min intervals during the night (22:00h – 07:00h). This enabled us to obtain numerous measurements while limiting interference with activity or sleep. No participants were allowed to record 24-hour ambulatory blood pressure while on an overnight shift. As a result, individuals who were working during the night at the time of the study were excluded. Participants were also advised to avoid planned exercise while wearing the device and to report periods of physical activity that occurred during the period using a daily activity record book. We assessed successful 24-hour blood pressure recordings using both the European Society of Hypertension (ESH) practice guidelines for ambulatory blood pressure monitoring(30), that is, interval between measurements not exceeding 30 minutes, at least 70% of expected number of readings obtained, at least 40 readings obtained over 24 hours, no more than 2 hours with missing readings, and no consecutive hours with missing readings. If ambulatory blood pressure recordings did not meet all of these criteria, they were not considered in the final analysis. We summarized 24-hour BP measurements as 24-hour average, daytime, and night-time average BP systolic and diastolic.

Biostatistical methods

Sample size calculation—Using prior data(31), we estimated that a sample size of at least 250 individuals (125 HIV positive, 125 HIV negative) would provide more than 90% power to detect a mean difference in continuous 24-hour blood pressure of 5 mmHg between the groups.

We examined distributions of socio-demographic, behavioural and clinical characteristics between HIV positive and HIV negative individuals. These characteristics were summarized using counts and percentages for categorical variables, and medians (and interquartile ranges) for continuous variables. Chi-square tests and Wilcoxon tests were used to examine bivariate differences in categorical and continuous variables, respectively.

Next, we computed the proportion with hypertension (high blood pressure) profiles in PLHIV and HIV negative individuals and compared these differences using chi-square tests. High blood pressure profiles were grouped as follows using the 2014 guidelines established by the European Society of Hypertension ABPM(30): 24-hour hypertension (defined as a 24-hour average of 130/80 mmHg), day hypertension (defined as a daytime average of 135/85mmHg), and night-time (nocturnal) hypertension (defined as a night-time average of 120/70 mmHg). To determine the association of HIV status with average continuous blood pressure values, we fitted crude and multivariable linear regression models with HIV as an independent variable. We then fitted crude and multivariable Poisson regression models with robust error variance to obtain prevalence ratios and corresponding 95% confidence intervals of the associations between HIV status and binary hypertension outcomes. Covariates adjusted for included socio-demographic characteristics (e.g., age, sex, marital status, level of education, occupation, and type of cooking fuel) as well as clinical and lifestyle factors (body mass index, and current cigarette smoking status).

We further conducted a sub-group analysis among only PLHIV to evaluate associations between detectable viral load, and continuous and binary blood pressure outcomes. All statistical tests were two-sided with alpha set at 0.05. All analyses were performed using STATA 14 (Stata Corp, College Station, TX, USA).

Ethical consideration

The procedures for all the study activities were approved by Makerere University School of Medicine, Research Ethics Committee (SOM-REC: Ref 2018–019) and Uganda National Council of Science and Technology (UNCST: Ref SS 4531). Administrative authorization was provided by the Nakaseke District health officer as well as the respective hospital and clinic heads. Before carrying out study procedures, written informed consent was obtained from literate participants, or thumb-printed and signed by a witness for participants who could not read or write.

Results

Patient socio-demographic characteristics

306 participants met the ambulatory blood pressure monitoring criteria and were included in the final analysis, while 222 were excluded for not fulfilling ambulatory blood pressure monitoring criteria. Distributions of most socio-demographic variables characteristics did not differ substantially between excluded individuals and those included in the final analytic sample for (see Supplementary Table 1).

A total of 140 HIV positive participants and 166 HIV negative individuals had successful 24-hour BP recordings and were included in final analysis. The median age among HIV positive participants was 45 years (IQR: 36, 53) and 44.5 years (IQR: 31, 57) among HIV negative participants. Majority of the participants were female (70% of HIV positive, and 81% HIV negative individuals). Median body mass index was significantly lower among HIV positive participants compared to HIV negative individuals: 20.91 (IQR: 19.15– 24.52) kg/m² compared to 22.99 (IQR: 21.18– 25.79) kg/m²; $p < 0.001$ (Table 1), with more HIV positive participants being underweight (18.8% vs. 4.6%). Most participants were non-smokers.

In Table 2, we describe the clinical characteristics of HIV positive participants—all were on ART. The majority had been on ART for a duration of less than 10 years and none reported a history of recent opportunistic infections like recurrent pneumonia, or candidiasis. Of 139 HIV positive participants for whom viral load information was available, 123 (88%) had undetectable viral load. Furthermore, HIV positive individuals were mainly on ART regimens consisting of Lamivudine and nucleoside/nucleotide reverse transcriptase inhibitors. Only six participants reported use of antihypertensive medication.

In Table 3, we show the distributions of continuous blood pressure measurements and binary hypertension according to HIV status. Median overall 24-hour systolic blood pressure was significantly lower in HIV positive participants than in their HIV negative counterparts: 110.4 mmHg (IQR: 105.7, 118.7) vs. 117.7 (IQR: 110.8, 129.8), $p < 0.001$. Similarly, the overall median 24-hour diastolic blood pressure was 2.6 mmHg lower among HIV seropositive participants compared to HIV seronegative participants ($p = 0.004$). The median day systolic BP and diastolic BP were 6.4 mmHg and 2.6 mmHg respectively lower in HIV positive participants compared to HIV negative participants. The prevalence of day hypertension was higher among HIV negative participants than among HIV positive participants (25.3% vs. 15.0%, $p = 0.026$). HIV positive participants had 8.5 mmHg lower median night systolic BP ($p < 0.001$) and 3.4 mmHg lower median night diastolic BP ($p < 0.001$) compared to HIV negative participants. The prevalence of nocturnal hypertension was higher among HIV negative participants than HIV positive individuals (34.9% vs 18.6%, $p = 0.001$).

After adjusting for socio-demographic, body mass index and lifestyle factors, both continuous 24-hour systolic BP and night systolic BP was significantly lower among HIV positive participants compared to HIV negative participants. However, there was no statistically significant difference in continuous 24-hour diastolic BP, day diastolic BP,

or night diastolic BP between the groups (Table 4). When we limited the analyses to non-smokers, the estimates were slightly attenuated (not shown). No statistically significant interactions were observed between HIV status and the continuous body mass index for 24-hour, day and night blood pressure measurements (not shown). After adjustment for covariates, we did not observe statistically significant differences in the prevalence ratios of binary hypertension for HIV positive individuals compared to HIV negative (Table 5).

HIV positive sub-group analysis

Results of the sub-group analysis among HIV positive individuals with a detectable viral load were in the direction of higher continuous 24-hour, day and night blood pressure measurements compared to those with undetectable viral load; however, these results were not statistically significant (Supplementary Table 2). This could be attributed to reduced statistical power, as only 16 HIV positive individuals had detectable viral load.

Discussion

In this study, we found that after adjustment for covariates, continuous 24-hour, day and night systolic blood pressure measurements were lower in HIV positive individuals established on ART compared to HIV negative individuals living within the same community in rural Uganda. Moreover, nocturnal (night) hypertension occurred in nearly 35% and 19% of HIV negative and HIV positive participants respectively. Nocturnal hypertension cannot be detected using conventional office BP measurements, underscoring the importance of recommendations from the National Institute for Health and Clinical Excellence (NICE) and European Society for Hypertension and Cardiology to integrate ambulatory blood pressure measurement in the diagnosis and monitoring of high blood pressure (32). Our findings are consistent with two large population-based studies in Africa that used conventional BP measurement and showed that the prevalence of hypertension was nearly 50% higher in the HIV negative than in HIV positive individuals (20, 33)

However, these findings are contrary to what has previously been described in most previous studies where HIV has been associated with increased risk of hypertension and cardiovascular risk in general(34, 35). Also, studies done in middle and high-income settings found no difference in ambulatory blood pressure measurements between HIV positive and HIV negative individuals. For example, a study done in South Africa found no difference in mean day-time systolic blood pressure and diastolic blood pressure between HIV positive and HIV negative groups (25). However, night-time blood pressure was higher in the HIV positive group than the HIV negative group (25). Similarly, a systematic review and meta-analysis published in 2016 found no significant difference in mean 24-hour, day-time and night-time blood pressure profiles between HIV positive and HIV negative participants (23).

The mechanisms for how HIV might influence blood pressure are not fully understood but may include shared behavioural risk factors, biological effects (such as inflammation/immune activation) or a result of side effects of ART(7). For example, in our study, HIV positive individuals were more likely to be smokers than those who were HIV negative. However, body mass index was lower in those with HIV than in those without HIV. Reduced

rates of obesity among HIV positive individuals compared to HIV negative individuals have also been reported in other studies in Africa (20).

The severity of HIV at presentation and/or the level of control after initiation of ART may also influence hypertension/CVD risk (7). In our study, HIV was well-controlled (all were on ART) and only a few HIV patients had a history of opportunistic infections. ART (particularly protease inhibitors) has been implicated as an independent risk factor for hypertension (7). In our study, most of the HIV positive participants were on either Tenofovir or Zidovudine and Efavirenz. Some of the antiretroviral agents that have been classically associated with high risk of hypertension or cardiovascular disease, such as boosted protease inhibitors (Lopinavir/ritonavir and Atazanavir/ritonavir) are used as second-line drugs in Uganda (36), but were minimally used in our study participants. Thus, the high level of HIV control with relatively benign agents may explain the lack of association between HIV positive status and hypertension in our study population.

Another explanation for the lower blood pressure measurements in HIV positive individuals compared to HIV negative individuals might relate to the health system effect. HIV positive participants in our sample have regular contact with the healthcare system where they receive regular health education messages in addition to HIV care (36). These include behavioural change advice like reduction of salt intake, weight reduction and regular physical exercise(36). These lifestyle modifications may have an impact on body mass index and blood pressure. For example, in a study conducted at an integrated chronic disease clinic in Uganda, among HIV positive individuals with or without hypertension and HIV negative with hypertension, blood pressure control was better among HIV positive than among HIV negative individuals at follow-up (37).

Our study has a number of limitations. First, this was a cross-sectional study and thus, we cannot draw conclusions on the causal effect of HIV status on blood pressure profiles. Second, participants in our study were predominantly rural dwellers, so our findings may not be generalizable to urban settings within Uganda. Third, the majority of our study participants were virologically suppressed (approximately 88%), and thus our study was not powered enough to assess the impact of the HIV virus on blood pressure. Fourth, we did not conduct blood tests for lipid profile, random or fasting glucose, renal function tests (urea and creatinine), urinalysis and 24-hour urine excretion or imaging including echocardiography, ECG and assess for carotid intima media thickness. This information would help to better characterize risks associated with the different BP profiles and rule out other comorbidities that might affect BP. Nonetheless, we used an extensive questionnaire to assess for comorbidities as well as patient medical records. Fifth, due to our relatively modest sample size, we were limited in performing detailed multivariable analysis of binary hypertension variables in the whole group, and within the HIV subgroup. Lastly, it is possible that men and women may differ in ways that significantly influence the association of HIV with blood pressure, yet our sample population was predominantly female.

In this study, we have demonstrated that among a rural Ugandan population of HIV positive individuals, the majority of whom are on ART and virologically suppressed, blood pressure is lower compared to HIV negative individuals, and the prevalence of catastrophic BP

profiles like nocturnal hypertension is markedly lower. However, there is still need for large prospective studies to better understand the cause and mechanistic pathways of hypertension and other risky BP profiles in people living with HIV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We acknowledge the skilled assistance of the research assistants Kukunda Rebecca and Chemutayi Sarah, as well as the contributions of all the participants, members of staff of the Nakaseke Hospital and other health centers in Nakaseke district. We are grateful to Maria Musisi, Maria Gorreti and Paula M. Namayanja (Makerere University-John Hopkins Research Collaboration) for providing study regulatory monitoring support. We acknowledge the management of African Community Center for Social Sustainability (ACCESS) for supporting the team during data collection.

Funding statement

This project was supported by NIH Research Training Grant (# D43 TW009340) funded by the NIH Fogarty International Center, NINDS, NIMH, and NHBLI. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Petersen M, Balzer L, Kwarsiima D, Sang N, Chamie G, Ayieko J, et al. Association of Implementation of a Universal Testing and Treatment Intervention With HIV Diagnosis, Receipt of Antiretroviral Therapy, and Viral Suppression in East Africa. *JAMA*. 2017;317(21):2196–206. [PubMed: 28586888]
2. UNAIDS. HIV AND AIDS IN EAST AND SOUTHERN AFRICA REGIONAL OVERVIEW. 2019.
3. Currier JS, Taylor A, Boyd F, Dezii CM, Kawabata H, Burtcel B, et al. Coronary heart disease in HIV-infected individuals. *Journal of acquired immune deficiency syndromes (1999)*. 2003;33(4):506–12. [PubMed: 12869840]
4. Durand M, Sheehy O, Baril J-G, Leloir J, Tremblay CL. Association Between HIV Infection, Antiretroviral Therapy, and Risk of Acute Myocardial Infarction: A Cohort and Nested Case–Control Study Using Québec’s Public Health Insurance Database. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2011;57(3):245–53. [PubMed: 21499115]
5. Triant VA. Cardiovascular disease and HIV infection. *Curr HIV/AIDS Rep*. 2013;10(3):199–206. [PubMed: 23793823]
6. Freiberg MS, Chang C-CH, Kuller LH, Skanderson M, Lowy E, Kraemer KL, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med*. 2013;173(8):614–22. [PubMed: 23459863]
7. Fahme SA, Bloomfield GS, Peck R. Hypertension in HIV-Infected Adults. *Hypertension*. 2018;72(1):44–55. [PubMed: 29776989]
8. Islam F, Wu J, Jansson J, Wilson D. Relative risk of cardiovascular disease among people living with HIV: a systematic review and meta-analysis. *HIV Medicine*. 2012;13(8):453–68. [PubMed: 22413967]
9. Policarpo S, Rodrigues T, Moreira AC, Valadas E. Cardiovascular risk in HIV-infected individuals: A comparison of three risk prediction algorithms. *Revista Portuguesa de Cardiologia (English edition)*. 2019;38(7):463–70.
10. Husain NE, Noor SK, Elmadhoun WM, Almobarak AO, Awadalla H, Woodward CL, et al. Diabetes, metabolic syndrome and dyslipidemia in people living with HIV in Africa: re-emerging challenges not to be forgotten. *HIV AIDS (Auckl)*. 2017;9:193–202. [PubMed: 29184449]

11. Ataro Z, Ashenafi W, Fayera J, Abdosh T. Magnitude and associated factors of diabetes mellitus and hypertension among adult HIV-positive individuals receiving highly active antiretroviral therapy at Jugal Hospital, Harar, Ethiopia. *HIV AIDS (Auckl)*. 2018;10:181–92. [PubMed: 30349400]
12. Palma AM, Rabkin M, Nuwagaba-Biribonwoha H, Bongomin P, Lukhele N, Dlamini X, et al. Can the Success of HIV Scale-Up Advance the Global Chronic NCD Agenda? *Global heart*. 2016;11(4):403–8. [PubMed: 27938826]
13. Collaborators GBDRF. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet (London, England)*. 2016;388(10053):1659–724.
14. Angkurawaranon C, Nitsch D, Larke N, Rehman AM, Smeeth L, Addo J. Ecological Study of HIV Infection and Hypertension in Sub-Saharan Africa: Is There a Double Burden of Disease? *PloS one*. 2016;11(11):e0166375–e. [PubMed: 27855194]
15. Kalyesubula R, Kayongo A, Semitala FC, Muhanguzi A, Katantazi N, Ayers D, et al. Trends and level of control of hypertension among adults attending an ambulatory HIV clinic in Kampala, Uganda: a retrospective study. *BMJ Global Health*. 2016;1(3):e000055.
16. Ryscavage P, Still W, Nyemba V, Stafford K. Prevalence of Systemic Hypertension Among HIV-Infected and HIV-Uninfected Young Adults. *Open Forum Infect Dis*. 2017;4(Suppl 1):S59–S.
17. önen NF, Overton ET, Seyfried W, Stumm ER, Snell M, Mondy K, et al. Aging and HIV Infection: A Comparison Between Older HIV-Infected Persons and the General Population. *HIV Clinical Trials*. 2010;11(2):100–9. [PubMed: 20542846]
18. Benzekri NA, Seydi M, N. Doye I, Toure M, Sy MP, Kiviat NB, et al. Increasing prevalence of hypertension among HIV-positive and negative adults in Senegal, West Africa, 1994–2015. *PLOS ONE*. 2019;13(12):e0208635.
19. Dillon DG, Gurdasani D, Riha J, Ekoru K, Asiki G, Mayanja BN, et al. Association of HIV and ART with cardiometabolic traits in sub-Saharan Africa: a systematic review and meta-analysis. *Int J Epidemiol*. 2013;42(6):1754–71. [PubMed: 24415610]
20. Malaza A, Mossong J, Bärnighausen T, Newell M-L. Hypertension and Obesity in Adults Living in a High HIV Prevalence Rural Area in South Africa. *PLOS ONE*. 2012;7(10):e47761. [PubMed: 23082211]
21. Piper MA, Evans CV, Burda BU, Margolis KL, O'Connor E, Whitlock EP. Diagnostic and Predictive Accuracy of Blood Pressure Screening Methods With Consideration of Rescreening Intervals: A Systematic Review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2015;162(3):192–204. [PubMed: 25531400]
22. Drain PK, Hong T, Hajat A, Krows M, Govere S, Thulare H, et al. Integrating hypertension screening at the time of voluntary HIV testing among adults in South Africa. *PLOS ONE*. 2019;14(2):e0210161. [PubMed: 30735518]
23. Kent ST, Bromfield SG, Burkholder GA, Falzon L, Oparil S, Overton ET, et al. Ambulatory Blood Pressure Monitoring in Individuals with HIV: A Systematic Review and Meta-Analysis. *PloS one*. 2016;11(2):e0148920–e. [PubMed: 26882469]
24. Parati Ga; Stergiou George; O'Brien Eoin; Asmar Roland; Beilin Lawrence; Bilo Grzegorz; Clement Denis; de la Sierra Alejandro; de Leeuw Peter; Dolan Eamon; Fagard Robert; Graves John; Head Geoffrey A.; Imai Yutaka; Kario Kazuomi; Lurbe Empar; Mallion Jean-Michel; Mancina Giuseppe; Mengden Thomas; Myers Martin; Ogedegbe Gbenga; Ohkubo Takayoshi; Omboni Stefano; Palatini Paolo; Redon Josep; Ruilope Luis M.; Shennan Andrew; Staessen Jan A.; vanMontfrans Gert; Verdecchia Paolo; Waeber Bernard; Wang Jiguang; Zanchetti Alberto; Zhang Yuqing. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *Journal of Hypertension*. 2014;32(7):1359–66. [PubMed: 24886823]
25. Borkum M, Wearne N, Alfred A, Dave JA, Levitt NS, Rayner B. Ambulatory blood pressure profiles in a subset of HIV-positive patients pre and post antiretroviral therapy. *Cardiovasc J Afr*. 2014;25(4):153–7. [PubMed: 25192297]
26. Borkum MS, Heckmann JM, Manning K, Dave JA, Levitt NS, Rayner BL, et al. High prevalence of “non-dipping” blood pressure and vascular stiffness in HIV-infected South Africans on antiretrovirals. *PloS one*. 2017;12(9):e0185003–e. [PubMed: 28931072]

27. Kasper P, Phiri S, Chaweza T, Tweya H, Neuhaan F, Steffen HM. 24-H-AMBULATORY BLOOD PRESSURE MONITORING IN HIV(+) - INDIVIDUALS IN SUB-SAHARAN AFRICA: FEASIBILITY AND PRELIMINARY RESULTS. *Journal of Hypertension*. 2019;37:e126.
28. Ivy A, Tam J, Dewhurst MJ, Gray WK, Chaote P, Rogathi J, et al. Ambulatory Blood Pressure Monitoring to Assess the White-Coat Effect in an Elderly East African Population. *The Journal of Clinical Hypertension*. 2015;17(5):389–94. [PubMed: 25690267]
29. Statistics UBo. The national population and housing census 2014–main report. UBOS Kampala, Uganda; 2016.
30. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G, et al. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *Journal of Hypertension*. 2014;32:1359. [PubMed: 24886823]
31. Schillaci G, Maggi P, Madeddu G, Pucci G, Mazzotta E, Penco G, et al. Symmetric ambulatory arterial stiffness index and 24-h pulse pressure in HIV infection: results of a nationwide cross-sectional study. *Journal of hypertension*. 2013;31(3):560–7. [PubMed: 23282895]
32. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M, et al. Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31(7):1281–357. [PubMed: 23817082]
33. Kwarisiima D, Balzer L, Heller D, Kotwani P, Chamie G, Clark T, et al. Population-Based Assessment of Hypertension Epidemiology and Risk Factors among HIV-Positive and General Populations in Rural Uganda. *PLoS one*. 2016;11(5):e0156309–e. [PubMed: 27232186]
34. Xu Y, Chen X, Wang K. Global prevalence of hypertension among people living with HIV: a systematic review and meta-analysis. *Journal of the American Society of Hypertension*. 2017;11(8):530–40. [PubMed: 28689734]
35. Nduka C, Stranges S, Sarki A, Kimani P, Uthman O. Evidence of increased blood pressure and hypertension risk among people living with HIV on antiretroviral therapy: a systematic review with meta-analysis. *Journal of Human Hypertension*. 2016;30(6):355–62. [PubMed: 26446389]
36. Health Mo. CONSOLIDATED GUIDELINES FOR PREVENTION AND TREATMENT OF HIV IN UGANDA. 2016.
37. Kwarisiima D, Atukunda M, Owaraganise A, Chamie G, Clark T, Kabami J, et al. Hypertension control in integrated HIV and chronic disease clinics in Uganda in the SEARCH study. *BMC Public Health*. 2019;19(1):511. [PubMed: 31060545]

Summary Table

What is known about the topic?

HIV infection has been associated with increased risk of hypertension.

24-hour risky ambulatory blood pressure profiles including nocturnal hypertension and non-dipping blood pressure profiles are more prevalent among HIV positive than among HIV negative individuals.

What this study adds:

Contrary to the existing literature, 24-hour blood pressure is lower among people living with HIV established on ART, compared to HIV negative individuals living within the same community in rural Uganda.

People living with HIV were also less likely to have overt hypertension and nocturnal hypertension than HIV negative individuals.

Table 1:

Background characteristics of participants according to HIV status in rural Uganda

Variable	HIV negative (n = 166)	HIV positive (n = 140)	P-value
Age, years, median (IQR)	44.5 (31, 57)	45 (36,53)	0.719
Sex: Female, n (%)	134 (80.72%)	98 (70.0%)	0.029
Body mass index in kg/m ² , median (IQR)	22.99 (21.18, 25.79)	20.91 (19.15, 24.52)	<0.001
Body mass index categories, n (%)			
Underweight (<18.5 kg/m ²)	7 (4.6%)	24 (18.8%)	<0.001
Normal weight (18.5–24.9 kg/m ²)	95 (62.5%)	77 (60.2%)	
Overweight/obese (≥ 25 kg/m ²)	50 (32.9%)	27 (21%)	
Marital status, n (%)			
Single	11 (6.6%)	6 (4.3%)	0.050
Married/ Cohabiting	103 (62.1%)	71 (50.7%)	
Separated/ Divorced	27 (16.3%)	40 (28.6%)	
Widow/widower	25(15.1%)	23 (16.4%)	
Education level completed, n (%)			
None	21 (12.7%)	29 (20.7%)	0.009
Primary	94 (56.6%)	88 (62.9%)	
Secondary	40 (24.1%)	21 (15.0%)	
Post-Secondary	11 (6.6%)	2 (1.4%)	
Employment, n (%)			
Government/Private sector	17 (10.2%)	8 (5.7%)	0.006
Commercial activities	20 (12.1%)	21 (15.0%)	
Worker	2 (1.2%)	2 (1.4%)	
Peasant/Farmer	108 (65.1%)	105 (75.0%)	
Housewife/Other	0 (0.0%)	1 (0.7%)	
Missing	19 (11.5%)	3 (2.1%)	
Fuel source for cooking, n (%)			
Wood	73 (44.0%)	54 (38.6%)	0.441
Charcoal	87 (52.4%)	83 (59.3%)	
Other	6 (3.6%)	3 (2.1%)	
Current cigarette smoker, n (%)			
Non-Smoker	162 (97.6%)	128 (91.4%)	0.020
Smoker	4 (2.4%)	12 (8.6%)	

IQR: Interquartile Range

Table 2:

Clinical characteristics of HIV positive participants in rural Uganda

Variables	n (%)
Current anti-retroviral therapy use	
Yes	140 (100)
No	0 (0)
Duration on anti-retroviral therapy (in years)	
< 1	6 (4.29)
1 – 4	58 (41.43)
5 – 9	57 (40.71)
10 +	13 (9.29)
Missing	6 (4.29)
Viral Load	
Undetectable	123 (87.86)
Detectable	16 (11.43)
Missing	1 (0.71)
Baseline CD4+T (cells/mm ³)	
<200	17 (12.14)
200–499	41 (29.29)
500	7 (5)
Missing	75 (53.57)
History of opportunistic infections [‡]	
Recurrent pneumonia	0 (0)
Candidiasis	0 (0)
Pneumocystis Carini Pneumonia	0 (0)
Kaposi sarcoma	1 (0.71)
Tuberculosis	4 (2.86)
Prophylaxis Treatment [‡]	
Septrin	130 (92.86)
Dapsone	3 (2.14)
Missing	7 (5)
Anti-retroviral therapy drugs [‡]	
Lamivudine	140 (100)
Nucleoside/nucleotide reverse transcriptase inhibitors	140 (100)
Non-nucleoside/nucleotide reverse transcriptase inhibitors	134 (95.71)
Proteinase inhibitors	4 (2.86)
Integrase inhibitors	1 (0.71)

[‡]indicates that items are not mutually exclusive

Table 3:

Distribution of continuous blood pressure measurements and hypertension according to HIV status in rural Uganda

Blood pressure measurements (mm/Hg)	HIV negative (n = 166)	HIV positive (n = 140)	P-value
24-hour blood pressure			
24-hour systolic (<i>median, IQR</i>)	117.7 (110.8, 129.8)	110.4 (105.7, 118.7)	< 0.001
24-hour diastolic (<i>median, IQR</i>)	71.9 (67.2, 78.1)	69.2 (65.0, 74.9)	0.004
24-hour hypertension, <i>n (%)</i>	48 (28.9%)	23 (16.4%)	0.010
Daytime			
Day systolic (<i>median, IQR</i>)	121.6 (114.7, 132)	115.2 (110.3, 125.1)	<0.001
Day diastolic (<i>median, IQR</i>)	75.5 (70.6, 81.4)	72.9 (68.3, 77.8)	0.009
Day hypertension, <i>n (%)</i>	42 (25.3%)	21 (15.0%)	0.026
Night (nocturnal)			
Night systolic (<i>median, IQR</i>)	107.3 (98, 119.9)	98.8 (91.8, 108.8)	<0.001
Night diastolic (<i>median, IQR</i>)	63.1 (57.1, 70.6)	59.7 (53.9, 66.3)	0.001
Night hypertension, <i>n (%)</i>	58 (34.9%)	26 (18.6%)	0.001
Systolic nocturnal dipping (<i>median, IQR</i>)	11.35 (8.1, 15.5)	13.45 (9.15, 19.0)	0.084

BP, blood pressure; IQR: Interquartile Range

24-hour hypertension is defined as systolic BP \geq 130 mmHg and/or diastolic BP \geq 80mmHg; Day hypertension is defined as systolic BP \geq 135 mmHg and/or diastolic BP \geq 85mmHg; Nocturnal hypertension is defined as systolic BP \geq 120 mmHg and/or diastolic BP \geq 70mmHg; Systolic nocturnal dipping is defined as the decrease in BP during night-time sleep relative to BP during daytime activity, calculated as: [average 24 hour day systolic BP - average 24 hour night systolic BP]/ [average 24 hour day systolic BP].

Table 4:

Differences in continuous blood pressure measurements between HIV positive individuals and HIV negative individuals in rural Uganda—results of linear regression

Blood pressure measurements (mm/Hg)	Crude: (Difference in mmHg, 95% CI)	Adjusted for socio-demographic factors: (Difference in mmHg, 95% CI)	Adjusted for socio-demographic and lifestyle factors: (Difference in mmHg, 95% CI)
24-hour BP measurements			
24-hour systolic	-7.62 (-10.89, -4.36)*	-4.67 (-7.76, -1.57)*	-3.63 (-6.89, -0.37)*
24-hour diastolic	-3.04 (-5.11, -0.99)*	-1.21 (-3.36, 0.95)	0.00 (-2.31, 2.30)
Day BP measurements			
Day systolic	-6.70 (-10.02, -3.38)*	-3.68 (-6.85, -0.51)*	-2.54 (-5.91, 0.82)
Day diastolic	-2.83 (-4.97, -0.70)*	-0.94 (-3.21, 1.33)	0.35 (-2.05, 2.75)
Night BP measurements			
Night systolic	-8.69 (-12.46, -4.91)*	-5.77 (-9.54, -2.00)*	-5.77 (-9.34, -2.20)*
Night diastolic	-3.58 (-5.75, -1.41)*	-1.76 (-4.01, 0.49)	-0.88 (-3.31, 1.56)
% Systolic nocturnal dipping	2.62 (1.12, 4.13)*	2.55 (0.86, 4.24)*	2.70 (0.94, 4.47)*

BP: Blood Pressure; CI: Confidence Interval.

Adjusted models include socio-demographic (age, sex, marital status, level of education, occupation, type of cooking fuel), and clinical and lifestyle factors (body mass index, cigarette smoking).

* Asterisk denotes statistical significance (i.e., $p < 0.05$)

Table 5:

Prevalence ratios for associations of HIV status with binary hypertension variables in rural Uganda—results of Poisson regression

Types of hypertension	Crude: (Prevalence ratio, 95% CI)	Adjusted for socio-demographic factors: (Prevalence ratio, 95% CI)	Adjusted for socio-demographic and lifestyle factors: (Prevalence ratio, 95% CI)
24-hour hypertension	0.57 (0.36, 0.89) *	0.84 (0.50, 1.40)	0.89 (0.51, 1.56)
Day hypertension	0.59 (0.37, 0.95) *	1.06 (0.60, 1.89)	1.20 (0.64, 2.24)
Night hypertension	0.53 (0.35, 0.80) *	0.72 (0.46, 1.14)	0.79 (0.48, 1.29)

CI: Confidence Interval

* Asterisk denotes statistical significance (i.e., $p < 0.05$)