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Blood pressure in relation to the World Health Organization AIDS clinical staging among adults living in rural Kenya

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Abstract

Introduction: Human immunodeficiency virus (HIV) is an independent risk factor of arterial hypertension. There is a limited data on blood pressure among HIV-positive patients living in rural areas in Africa according to the clinical progress of the disease. The aim of the study was to compare blood pressure (BP) parameters among HIV-positive adults with advanced and non-advanced HIV/acquired immunodeficiency syndrome (AIDS) living in rural Kenya.

Material and methods: In this prospective, two-center, cross-sectional study, we examined HIV-positive individuals visiting the outpatient department for a routine check-up. BP was measured by OMRON M2 Basic BP monitor (Omron, Japan) and clinical data was collected from patients' data charts. World Health Organization AIDS clinical stage (WACS) equal to 1 was defined as non-advanced HIV, while WACS equals 2, 3, or 4 were classified as advanced HIV. Data presented as median (interquartile range).

Results: From the total of 245 (female, 192; 78%) participants, 162 individuals presented non-advanced HIV disease, whereas 83 had advanced HIV. Both groups did not differ significantly regarding sex, age, time since HIV diagnosis, body mass index, waist circumference, use of antiretroviral treatment, nor presence of abnormal blood pressure. However, there were significant differences between patients with non-advanced HIV and advanced HIV in diastolic BP (DBP) [71 (64-77) vs. 81 (75-88); $p < 0.0001$], mean BP (MBP) [87 (80-94) vs. 95 (88-102); $p < 0.0001$], and pulse pressure (PP) [48 (42-56) vs. 43 (35-50); $p < 0.0001$]. A tendency, but not significant difference between study groups in systolic BP [119 (109-129) vs. 122 (114-133); $p = 0.07$] was observed.

Conclusions: HIV-positive patients with advanced form of HIV disease have higher DBP, MBP, and lower PP than individuals with non-advanced HIV living in rural Kenya.

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Key words: blood pressure, HIV, AIDS, Kenya, stage.

Introduction

Human immunodeficiency virus (HIV) infection causes the acquired immunodeficiency syndrome (AIDS), a progressively devastating process complicated by malnutrition, wasting, development of other infectious and neoplastic diseases, and shorter life duration [1, 2]. The epidemic of HIV/AIDS is a mayor public health challenge in sub-Saharan Africa,

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with up to 25 million HIV-positive individuals [3]. Due to efficacy of antiretroviral treatment (ART), HIV-positive patients tend to live longer, and cardiovascular diseases (CVD) became the mayor mortality cause in this population [4, 5]. HIV infection is recognized as an independent CVD risk factor [6]. HIV/AIDS promotes chronic inflammation process resulting in atherosclerosis [7], increases arterial wall stiffness [8], and the risk of arterial hypertension [9]. The risk of CVD in HIV/AIDS is negatively correlated with CD4+ count [10-12]. Moreover, HIV-positive patients are additionally more likely to develop arterial hypertension due to metabolic side effects of ART [13].

In sub-Saharan Africa, both HIV/AIDS and cardiology advanced diagnostics and treatments are limited. Therefore, an early health intervention is crucial among patients with HIV/AIDS and cardiovascular risk living in non-industrialized areas [14]. However, there is a limited data on blood pressure among HIV-positive patients living in rural areas in Africa according to the clinical progress of the disease. Possibly, one of those groups of patients requires more careful monitoring of blood pressure and early health interventions to prevent cardiovascular events, which cannot be efficiently treated in rural areas.

The aim of the study was to compare blood pressure parameters between HIV-positive adults with advanced and non-advanced forms of HIV/AIDS.

Material and methods

We performed prospective, two-center, cross-sectional study in rural Comprehensive Care Clinic (CCC) for HIV patients in Mutomo and Muthale Missionary Hospitals, Kitui County, Kenya. Data was collected in August and September 2016. The study team consisted of local staff and medical volunteers, who participated in the program "Treating with a mission" (leczymyzmisja.pl/en/) under the auspices of the Poznan University of Medical Sciences, Poznan, Poland. The local Bioethical Committee at the Strathmore University in Nairobi, Kenya approved the study protocol (permission reference number SU-IRB 0073/16), and each participant signed an informed consent before participation. In the case of illiteracy, oral informed consent in local language or Swahili was obtained by two CCC workers. In our study, adult HIV-positive patients visiting the outpatient clinic during a routine check-up visit were included and their data anonymized. All patients have been previously diagnosed in the CCC accordingly to the Kenyan HIV diagnostic guidelines [15]. Patients with newly diagnosed HIV-infection, e.g. acute retroviral infection, were excluded. Each participant underwent an interview with a local clinical consultant, clinical examination, anthropometric and blood pressure measurements, and heart rate assessment. Additional data such as World Health Organization (WHO) AIDS clinical stage (WACS), HIV treatment, and time since HIV diagnosis were collected from patients' data charts.

Anthropometric measurements were collected using body composition analyzer (TANITA BC-601, Illinois, USA), which allows to assess patient's body mass, body fat percentage, and abdominal fat level. Resting systolic (SBP) and diastolic blood pressure (DBP) were measured after 5 minutes of resting using OMRON M2 basic BP monitor (Omron, Japan) validated according to the international protocol of the European Society of Hypertension [16]. Blood pressure was measured after the participant had rested for at least five minutes and was seated comfortably with his back supported, legs uncrossed, and his feet flat on the floor. Clothing was removed from the arm, in which the cuff was placed. The arm was supported at heart level, with the palm facing up and the elbow slightly flexed. The patient was advised not to speak during the procedure. Different cuff sizes based on the upper arm circumference at the time of each measurement were used. After 2 minutes of rest, second measurement was performed, and the average measurement was used for statistical analysis. Heart rate (HR) was obtained by an AliveCor (AliveCor, USA), a system of electrode and a smartphone application called Kardia, which enables obtaining one-lead ECG from the user [17]. The mean blood pressure (MBP) was calculated according to MBP = 2/3 DBP + 1/3 SBP formula [18]. The pulse pressure (PP) was calculated according to PP = SBP – DBP method. To the final analysis, only completely fulfilled records were included. Abnormal blood pressure was defined as SBP ≥ 140 and/or > DBP ≥ 90.

In order to grade the progression of HIV infection, the WHO recommends using WACS [1], which is a four-grade system designed for developing countries with limited possibility to routinely assess CD4+ count. The WACS grading starts from the asymptomatic patients or with generalized lymphadenopathy (stage 1), through the presence of unexplained moderate to severe weight loss, ranges from mild to severe bacterial, viral and fungal infections (stages 2 and 3), and ends with the development of HIV wasting syndrome, severe generalized infection, and HIV-associated malignancy (stage 4). The clinical staging of HIV patients enrolled in our study was regularly evaluated by medical professionals working in both outpatient clinics. Since we included patients attending routine check-ups, our study group did not include patients with a condition requiring urgent hospitalization. We distinguished group of ART treatment used by each patient for at least one previous month. Additionally, we characterized each combination of ART prescribed.

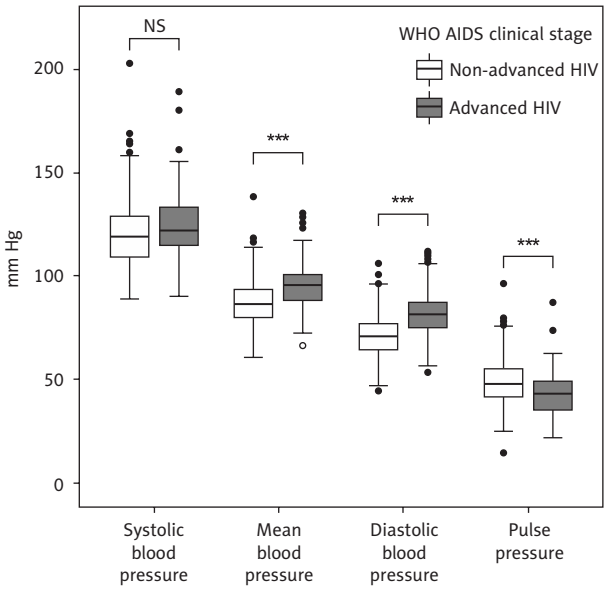
Data analysis

A statistical analysis was performed using STATISTICA 12.0 (StatSoft, USA). Normality of variables distribution was tested using Kolmogorov-Smirnov test with Lilliefors correction. Due to lack of normality, non-parametric tests were performed. We divided patients into two groups: patients with non-advanced form of HIV disease (stage 1 in WACS) and with advanced form of HIV disease (stage 2, 3, or 4 in WACS). Comparison of non-advanced with advanced HIV was made by Mann-Whitney test, and results shown as median and 25^{th}-75^{th} percentiles. In order to compare study groups in the presence of abnormal blood pressure, treatment χ^2 test

was used. To assess associations between blood pressure parameters and clinical features in study groups, Spearman rank correlation test was performed. Differences with p value < 0.05 were considered statistically significant. The figure was generated by using ggplot2 and ggthemes R packages [19].

Results

Out of 268 patients, we excluded 23 patients due to uncompleted records, which resulted in the total of 245 (female, 192; 78%) participants included in the study, aged 46 (range, 39-53), in the final analysis. All patients were using ART. The prescribed antiretroviral drugs were: nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) – lamivudine, abacavir, and zidovudine; non-nucleoside reverse transcriptase inhibitors (NNRTI) – efavirenz and nevirapine; reverse transcriptase inhibitor (RTI) – tenofovir; protease inhibitors (PI) – lopinavir and atazanavir. We noted following ART combinations: NRTI + NNRTI + RTI (n = 123), NRTI + NRTI + NNRTI (n = 97), NRTI + NRTI + PI (n = 22), NRTI + RTI + PI (n = 2), and NRTI in monotherapy (n = 1). General characteristics of the group is summarized in Table 1. One hundred and two patients presented with non-advanced HIV disease (WACS = 1), whereas 83 had advanced disease (WACS > 1): 23 had WACS = 2, 52 had WACS = 3, and eight had WACS = 4. Both groups did not differ significantly in sex, age, time since HIV diagnosis, age at HIV diagnosis, body



*NS – non-significant; ***p < 0.0001*

Figure 1. Comparison of blood pressure parameters between patients with non-advanced human immunodeficiency virus (HIV) disease and with advanced HIV. Boxplot: band inside the box – median, box – interquartile range (IQR), upper whisker: upper quartile + IQR, lower whisker: lower quartile – IQR

Table 1. Comparison of clinical features between asymptomatic and symptomatic human immunodeficiency virus (HIV)-positive patients. Data expressed as median (IQR) or n (%)

Parameter	All patients N = 245 (100%)	Non-advanced HIV n = 162 (66%)	Advanced HIV n = 83 (34%)	p-value
Sex – females, n (%)	192 (78)	131 (81)	61 (73)	0.18
Age (years)	46 (39-53)	45 (39-52)	47 (41-54)	0.05
Time since HIV diagnosis (years)	7 (5-9)	8 (5-9)	7 (6-9)	0.90
Age at HIV diagnosis (years)	38 (32-46)	38 (32-45)	39 (34-47)	0.06
BMI (kg/m^2)	21.1 (19.1-24.1)	21.3 (19.0-24.4)	20.9 (19.2-23.8)	0.85
Waist circumference (m)	0.78 (0.71-0.85)	0.78 (0.72-0.86)	0.77 (0.71-0.82)	0.11
Fat tissue (%)	28 (21-33)	29 (21-35)	26 (21-32)	0.06
Abdominal fat level, n	5 (3-7)	5 (3-7)	5 (3-7)	0.64
Heart rate (bpm)	76 (68-86)	76 (69-87)	77 (68-86)	0.81
PI, n (%)	24 (10)	18 (11)	6 (7)	0.33
RTI, n (%)	125 (51)	77 (48)	48 (58)	0.13
NNRTI, n (%)	220 (90)	143 (88)	77 (93)	0.27
Double NRTI, n (%)	119 (48)	84 (52)	35 (42)	0.15
NRTI + NNRTI + RTI, n (%)	123 (50)	75 (46)	48 (58)	0.09
NRTI + NRTI + NNRTI, n (%)	97 (40)	68 (42)	29 (35)	0.29
NRTI + NRTI + PI, n (%)	22 (9)	16 (10)	6 (7)	0.49
Abnormal BP, n (%)	35 (14)	20 (12)	15 (18)	0.23

BMI – body mass index, BP – blood pressure, IP – protease inhibitors, NNRTI – non-nucleoside reverse transcriptase inhibitors, NRTI – nucleoside reverse transcriptase inhibitors, RTI – reverse transcriptase inhibitors

Table 2. *R* Spearman rank correlation test results. Outcomes expressed as Spearman rank coefficients

Parameter	All patients *N* = 245 (100%)				Non-advanced HIV *n* = 162 (66%)				Advanced HIV *n* = 83 (33%)			
	SBP	DBP	PP	MBP	SBP	DBP	PP	MBP	SBP	DBP	PP	MBP
Age (years)	**0.27***	**0.13***	**0.21***	**0.21***	**0.25***	0.10	**0.24***	**0.19***	**0.29***	0.08	**0.33***	0.17
Time since HIV diagnosis (years)	–0.04	**–0.13***	0.6	–0.09	–0.03	–0.13	0.09	–0.09	–0.05	–0.10	0.02	–0.06
Age at the HIV diagnosis (years)	**0.29***	**0.17***	**0.20***	**0.24***	**0.27***	**0.16***	**0.22***	**0.24***	**0.30***	0.10	**0.32***	0.18
BMI (kg/m^2)	0.06	0.09	–0.01	0.08	0.07	0.11	0.03	0.10	0.01	0.08	–0.12	0.05
Waist circumference (m)	0.12	0.04	0.11	0.08	0.11	0.07	0.10	0.10	0.17	0.12	0.08	0.14
Fat tissue (%)	–0.04	0.02	–0.08	–0.01	–0.01	0.08	–0.08	0.04	–0.08	0.06	**–0.24***	0.01
Abdominal fat level, *n*	**0.26***	**0.18***	**0.14***	**0.23***	**0.27***	**0.19***	**0.18***	**0.24***	**0.27***	0.16	0.14	**0.22***
Heart rate (bpm)	–0.01	0.11	–0.14	0.07	0.04	0.14	–0.10	0.10	–0.11	0.12	**–0.27***	0.03
WACS	0.11	**0.39***	**–0.27***	**0.30***	–	–	–	–	–	–	–	–

**p < 0.05*

BMI – body mass index, DBP – diastolic blood pressure, MBP – mean blood pressure, PP – pulse pressure, SBP – systolic blood pressure

mass index (BMI), waist circumference, fat tissue percentage, abdominal fat level, HR, use of antiretroviral drugs, nor presence of abnormal blood pressure (Table 1). The comparison of blood pressure parameters of each group is presented in Figure 1. There were significant differences between patients with non-advanced HIV and advanced HIV in DBP [71 (64-77) vs. 81 (75-88); $p < 0.0001$], MBP [87 (80-94) vs. 95 (88-102); $p < 0.0001$], and PP [48 (42-56) vs. 43 (35-50); $p < 0.0001$]. A tendency, but not significant difference among study groups in SBP [119 (109-129) vs. 122 (114-133); $p = 0.07$] was observed. We found significant associations between blood parameters and age, age at HIV diagnosis, abdominal fat level, and WACS of participants (Table 2).

Discussion

In our study, we found that patients with advanced form of HIV infection had a higher DBP and MBP and lower PP than patients with non-advanced form of HIV. Moreover, a tendency in difference between both groups in SBP was noted. Most likely, the differences between study groups in MBP and PP were secondary to difference in DBP, while SBP did not differ significantly. There was no significant difference between both groups in the presence of abnormal blood pressure.

The development of arterial hypertension in HIV/AIDS is multifactorial. HIV infection as such leads to endothelial dysfunction, inflammatory state, dyslipidemia, and insulin resistance [10]. In individuals with developed immunosuppression, inflammatory foci may accelerate in endothelial and metabolic changes caused by HIV [11, 12]. Finally, ART was reported to cause endothelial dysfunction, dyslipidemia, and worsen glucose tolerance [10, 13]. All those outcomes may result in an escalation of atherosclerosis, which in consequence increases a CV risk in HIV-positive people [7]. An increase of arterial stiffness in HIV-positive individuals was associated with advanced form of infection, presence of metabolic syndrome, and age [8]. Since the risk of metabolic syndrome is augmented by HIV infection, both non-HIV inflammatory foci and ART indirectly influence arterial stiffness, which has a sequential effect on the development of arterial hypertension in HIV-positive population [9].

Njekela *et al.* reported negative association between progression of HIV/AIDS (assessed by CD4+ count and advanced WACS) and risk of hypertension among ART-naïve patients living in Tanzania [20]. Moreover, the study showed that clinical stage of the disease alone may result in arterial hypertension. In another study performed on Kenyan population, Bloomfield *et al.* demonstrated that low blood pressure (SBP < 100, DBP < 60 mm Hg) carries the highest mortality risk among HIV-positive patients [21]. High SBP was also significantly associated with increased mortality, but only among patients without advanced form of HIV/AIDS [21]. Nadir of CD4+ count during the history of HIV/AIDS was correlated negatively with WACS [22] and nadir of CD4+ was characterized as an independent predictor of sustained hypertension [23]. Additionally, Manner *et al.* concluded that delaying ART initiation in ART-naïve patients may cause additional risk of arterial hypertension [23]. Since CD4+ count is negatively correlated with risk of hypertension, we speculate that poor adherence to ART therapy may result in the progression of disease, decrease of CD4+, promotion of chronic inflammation leading to an increase of arterial wall stiffness [8] and consequently, an increase of DBP.

To exclude potential influence of ART on blood pressure, both groups were compared according to prescribed treatment and no significant difference was observed. However, the compliance of patient is unknown. It is possible that patients with advanced form of infection resulted in worse compliance than those of non-advanced group, which could lead to a lack of clinical improvement or progression of HIV/AIDS.

Interestingly, WACS alone had significant associations with DBP, MBP, and PP. Moreover, age, age at HIV diagnosis, and abdominal fat level were positively associated with

BP parameters. Abdominal fat level correlates with visceral adiposity measured by magnetic resonance imaging [24]. Visceral adiposity was associated with renin-angiotensin-aldosterone (RAA) system activation in HIV-positive population [25]. Therefore, the observed association between abdominal fat level and DBP, MBP, and PP may reflect on activation of RAA system by visceral fat tissue.

Unexplained weight loss and HIV wasting syndrome are the criteria of advanced HIV infection [1]. However, no significant differences in BMI, waist circumference, and fat tissue between both groups were observed. We suppose that most of the patients were assigned to the advanced HIV infection group due to occurrence of at least one viral, bacterial, or fungal infection, unexplained fever, etc.

We analyzed data of 245 HIV-positive adults, mostly middle-aged females living in rural areas of Kenya. All individuals were on ART. Asymptomatic and symptomatic groups did not differ significantly in sex, age, BMI, time since HIV diagnosis, and HIV treatment. The only differences between both groups appeared in DBP, MBP, and PP. The results of our study suggest that HIV/AIDS clinical stage may be associated with DBP as well as MBP and PP. Individuals with advanced-HIV infection living in rural Kenya may require more clinical attention for early diagnosis of hypertension.

Our study has several limitations. Firstly, we collected data cross-sectionally without a follow-up. Secondly, the collected data was limited. We have not collected data on hypertension risk factors, e.g. family history of smoking, alcohol, diet, physical activity, and type of occupation. This would require an engagement of additional CCC workers, which was practically impossible. Data on comorbidities in patients' records were sparse. Information found in medical charts included only two patients who were previously diagnosed as hypertensive and one suffered from diabetes. However, we speculate that these numbers may be underestimated. HIV-positive patients are encouraged to disclose all health-related problems in CCC, but some may not admit their comorbidities due to a lack of sense of necessity or fear of shame (e.g. alcohol problems). Data on anti-hypertensive treatment were not collected due to lack of information in patients' data charts. Arterial hypertension is a multifactorial disease, and the limitation of data is a flaw of this study. Nevertheless, the possible factors influencing BP may be related to HIV/AIDS progression. HIV-positive patients with arterial hypertension may likely characterize with poor adherence to treatment, leading to an increase of blood pressure and progression of the infection, which is reflected by a higher stage of WACS. Regardless of the limitation, our study underlines the necessity of vigilant monitoring of BP in patients with an advanced stage of HIV infection living in African rural areas.

Conclusions

HIV-positive patients with advanced form of HIV disease have higher DBP and MBP and lower PP than individuals with non-advanced HIV living in rural Kenya.

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Conflict of interest

The authors declare no conflict of interest with respect to the research, authorship, and/or publication of this article.

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