Cardiovascular Topics

Cardiovascular risk factors among people living with HIV in rural Kenya: a clinic-based study

Kenneth Juma, Roseanne Nyabera, Sylvia Mbugua, George Odinya, James Jowi, Mzee Ngunga, David Zakus, Gerald Yonga

Abstract

Objectives: To determine the prevalence of cardiovascular risk factors and their association with antiretroviral therapy (ART) among HIV-infected adults in a rural sub-county hospital in Kenya.

Methods: This was a descriptive survey of patient charts characterising cardiovascular risk among adult patients (> 18 years) at Ukwala sub-county hospital between June 2013 and January 2015. Post-stratification survey weights were applied to obtain prevalence levels. Adjusted odds ratios (AOR) for each variable related to cardiovascular risk factors were calculated using logistic regression models.

Results: Overall, the prevalence of diabetes mellitus was 0.4%, 0.3% of patients had had a previous cardiovascular event (heart attack or stroke), 40.4% had pre-hypertension, while 10.4% had stage 1 and 2.9% stage 2 hypertension. Up to 14% of patients had elevated non-fasting total cholesterol levels. Factors associated with hypertension were male gender (AOR 1.59, $p = 0.0001$), being over 40 years of age (AOR 1.78, $p = 0.0001$) and having an increased waist circumference (OR 2.56, $p = 0.0014$). Raised total cholesterol was more likely in those on tenofovir disoproxil fumarate (TDF) (AOR 2.2, $p = 0.0042$), azidothymidine (AZT) (AOR 2.5, $p = 0.0004$) and stavudine (D4T)-containing regimens (AOR 3.13, $p = 0.0002$).

Conclusions: An elevated prevalence of undiagnosed cardiovascular risk factors such as hypertension and raised total cholesterol levels was found among people living with HIV. There was an association between raised total cholesterol and nucleoside reverse-transcriptase inhibitor (NRTI)-based ART regimens. Our findings provide further rationale for integrating routine cardiovascular risk-factor screening into HIV-care services.

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With the use and effectiveness of antiretroviral therapy (ART), people with HIV are living longer.[1] Non-AIDS events, of which cardiovascular disease (CVD) mediated by inflammation and atherosclerosis predominate, are becoming more prevalent.[2,3] A meta-analysis found that people living with HIV have a significantly higher risk for CVD when compared to HIV-negative persons.[4] This may be due to traditional cardiovascular risk factors such as smoking and hypertension, which have been found to be increased in some HIV-positive cohorts,[2,5] as well as ART,[6] exposure to HIV itself or immune activation and a pro-inflammatory state induced by HIV,[7] or a combination of these factors.

Although there are accumulating data on cardiovascular risk factors in people living with HIV in developed countries,[3] there are limited data from Africa. We report on the prevalence of risk factors for CVD among HIV-infected adults enrolled in HIV care and treatment at a sub-county hospital in Kenya, and describe the association with ART.

Methods

This was a cross-sectional survey of patient charts characterising cardiovascular risk among adult patients (> 18 years) at Ukwala sub-county hospital between June 2013 and January 2015. Within this period, individuals with HIV attending Ukwala sub-county hospital for HIV care were screened for cardiovascular risk factors

as part of a pilot project for integration of non-communicable disease care into HIV programmes supported by Grand Challenge Canada (GCC).

Ethical approval for this study was obtained from the Maseno University ethics review committee. Data used in this study were obtained from patient charts routinely collected at the clinic, and a written informed consent was provided before screening by each participant while attending the HIV clinic. Confidentiality, anonymity and privacy of all participants were guaranteed at all levels of this study by excluding all unique identifiers for the participants.

Baseline assessment included demographic variables, risk factors for CVD and measurement of body mass index (BMI), blood pressure, non-fasting total cholesterol and random blood glucose levels. World Health Organisation (WHO) cardiovascular risk score was calculated for patients aged above 40 years[8] and the information included in the patients' medical record files. All people with HIV attending the Ukwala HIV clinic were included. Those who declined consent for the cardiovascular risk-factor screening and pregnant women were excluded.

Patients fulfilling national eligibility criteria (CD4 count > 350 cells/mm^3 at time of the study) were treated with standard ART according to national guidelines.[9] Standard regimens at that time included tenofovir, lamivudine and efavirenz (TNF/3TC/EFV) or zidovudine, lamivudine and efavirenz (AZT/3TC/EFV). Some were still receiving stavudine, lamivudine and efavirenz (D4T/3TC/EFV), which was being phased out at the time. A minority received a lopinavir/ritonavir (LPV/r)-containing regimen.

Prior to commencing CVD screening within the HIV clinics at Ukwala sub-county hospital, healthcare providers (including nurses, laboratory technologists, clinicians and data clerks) in the health facility received a two-day training, followed by regular intensive theoretical and practical skills training and mentoring in measuring and interpreting cardiovascular risk factors. The facility was also provided with regularly calibrated point-of-care diagnostic equipment for cardiovascular risk assessment.

Blood pressure (BP) was measured using a hospital-grade Omron M3® (Omron, Netherlands) digital automatic blood pressure machine. Hypertension diagnosis was based on standard guidelines, and included blood pressure measurements, medical history, physical examination, assessment of absolute cardiovascular risks (where deemed necessary by the examining physician) and laboratory investigations. A comprehensive assessment of BP involved multiple measurements taken on separate occasions, at least twice or three times, one or more weeks apart or sooner if the hypertension was severe.

Hypertension was defined as per the seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7)[10] as follows: pre-hypertension: systolic 120–139 mmHg, diastolic 80–89 mmHg; stage 1 hypertension: systolic 140–159 mmHg, diastolic 90–99 mmHg; stage 2 hypertension: systolic ≥ 160 mmHg, diastolic ≥ 100 mmHg, and those currently on antihypertensive drugs.

Total cholesterol and blood glucose levels were measured in the clinic using finger-prick blood by a Humansence® (Human, Wiesbaden, Germany) meter calibrated with a control strip on the first and after every 10th specimen. Raised total cholesterol level was defined according to US National Cholesterol Education Program ATP III guidelines.[11]

Data collection involved the extraction of data from the patients' charts using a standardised data tool by trained data clerks. Charts for patients who attended the clinic from June 2013 to January 2015 were targeted. Those with missing details on key variables such as cardiovascular risk-factor screening results and ART regimen were excluded from the data.

Detailed abstraction was then conducted on the remaining patients' charts using a data tool that was made up of four sections, including: (1) anthropometric measures (age, body mass index, waist circumference and blood pressure), (2) behavioural and biomedical cardiovascular risk factors (including smoking status, excessive use of alcohol and non-fasting total cholesterol level), (3) clinical information (such as on HIV infection and HIV treatment, ART regimen and duration), and (4) medical history. Data extracted were entered in a paper data tool then later transferred into an EpiData software version 3.1 for clean-up in readiness for analysis using SPSS software.

Statistical analysis

Statistical analysis was performed using SPSS software version 22 (IBM SPSS Statistics, Armonk, NY: IBM Corp). Descriptive statistics involved calculating the median and interquartile range (IQR) for continuous data and proportions for categorical variables. Comparisons of median duration between groups were done using the Mann–Whitney test with a 5% level of significance. Associations were assessed using a logistic regression model, and crude and adjusted odds ratios are reported with their corresponding confidence intervals.

Results

A total of 1 510 subjects was screened, of whom eight were excluded from analysis because of incomplete data (Fig. 1). Data collected included demographic variables, risk factors for CVD and determination of BMI, measurement of blood pressure, and non-fasting total cholesterol and random blood glucose levels. Cardiovascular risk score was calculated for those above 40 years using the WHO (Afri-E) risk-screening chart.[8]

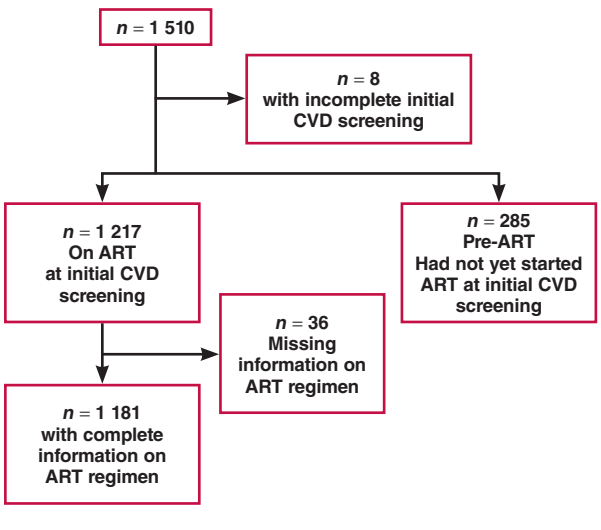

Fig. 1. Data flow chart for cardiovascular risk screening.

Table 1. Prevalence of cardiovascular risk factors among people living with HIV

Variables	*Frequency (n)*	*Overall %*
Age ≥ 40 years	716	47.4
Male gender	471	31.2
Current smokers	29	1.9
Increased waist circumference*	89	5.9
Total cholesterol ≥ 5.2 mmol/l	207	13.7
Body mass index ≥ 25 kg/m²	182	12.1
Random blood glucose ≥ 7.8 mmol/l	31	2.1
Known diabetes at screening	7	0.5
Cardiovascular risk score ≥ 10%	8	0.5
Pre-hypertension	609	40.4
Hypertension stage 1	157	10.4
Hypertension stage 2	43	2.9

*Females ≥ 90 cm, males ≥ 100 cm.

Of the subjects screened, 69% (1 036) were women. The median age was 30 (IQR 31–48) years and median CD4 count was 430 (IQR 308–574) cells/mm³; 79% of subjects were on ART with a documented regimen. Current smokers were 1.9% (29), whereas 0.4% (seven) had known diabetes and 0.3% (four) had had a previous cardiovascular event (heart attack or stroke).

The median BMI was 21 (IQR 20–23) kg/m² with 11% of subjects underweight, 12% overweight and 2% obese. Waist circumference was > 100 cm (102 cm) in 1% of men and > 90 cm (88 cm) in 7.5% of women (Table 1). The median duration on ART was 32.5 (17.4–50.6) months. Cardiovascular risk-factor distribution stratified by ART status is shown in Table 2.

Of the 1 502 individuals screened, 40.4% (609/1502) had pre-hypertension, 10.4% (157/1502) were stage 1 and 2.9% (43/1502) were stage 2 hypertension. In multivariate analysis, hypertension was associated with being male [adjusted OR 1.59 (1.26–2.01), $p = 0.0001$], being 40 years or older [adjusted OR 1.78 (1.44–2.21), $p = 0.0001$], and having an increased waist circumference [adjusted OR 2.56 (1.44–4.55), $p = 0.0014$].

While the association between lower CD4 count and prevalence of hypertension was not certain, lower CD4 count was indicative of a lower prevalence of hypertension among those with low CD4 counts. There was no association between hypertension and current ART regimen (Table 3). The median duration on ART was not significantly different for those with or without hypertension (Mann–Whitney test, $p = 0.6794$).

A total of 207 (14%) patients had an elevated non-fasting total cholesterol level (> 5.2 mmol/l). On multivariate analysis, being above 40 years of age [adjusted OR 1.95 (1.42–2.69), $p = 0.001$] and having an increased waist circumference [adjusted

Table 2. Cardiovascular risk factors stratified by ART status

CVD risk factors	*ART, n (%)*	*Pre-ART, n (%)*	p-*value*	*OR (95% CI)*
Male gender	396 (32.5)	74 (26.0)	0.0312	1.38 (1.03–1.84)
Age ≥ 40 years	629 (51.7)	87 (30.5)	0.0001	2.43 (1.85–3.21)
Current smokers	24 (2.0)	5 (1.8)	0.8100	1.13 (0.43–2.98)
Total cholesterol ≥ 5.2 mmol/l	186 (15.3)	19 (6.7)	0.0001	2.53 (1.55–4.13)
Body mass index ≥ 25 kg/m²	151 (12.4)	31 (10.9)	0.4761	1.16 (0.77–1.75)
Elevated waist circumference*	76 (6.2)	13 (4.6)	0.2786	1.39 (0.76–2.55)
Random blood glucose ≥ 7.8 mmol/l	25 (2.1)	5 (1.8)	0.7447	1.17 (0.45–3.10)
Cardiovascular risk score ≥ 10%	6 (0.5)	2 (0.7)	0.6630	0.70 (0.14–3.49)
Known diabetes	6 (0.5)	1 (0.4)	1.000	1.41 (0.17–11.70)
Hypertension	666 (54.7)	140 (49.3)	0.0985	1.24 (0.96–1.61)
Pre-hypertension	494 (47.3)	113 (44.0)	0.3415	1.14 (0.96–1.61)
Hypertension stage 1	132 (19.3)	24 (14.3)	0.1303	1.44 (0.90–2.30)
Hypertension stage 2	40 (6.6)	3 (2.0)	0.0291*	3.48 (1.06–11.42)

*Females ≥ 90 cm, males ≥ 100 cm; Fischer's exact two-sided test.

Table 3. Unadjusted and adjusted odds ratios for hypertension

	Unadjusted OR		*Adjusted OR*	
Characteristic	*OR (95% CI)*	p-*value*	*OR (95% CI)*	p-*value*
Male gender	1.65 (1.32–2.06)	0.0001	1.68 (1.32–2.14)	0.0001
Age ≥ 40 years	2.06 (1.67–2.53)	0.0001	1.78 (1.43–2.22)	0.0001
Current smokers	1.42 (0.67–3.02	0.3653	1.02 (0.47–2.24)	0.9574
Body mass index ≥ 30 kg/m²	3.14 (1.35–7.31)	0.0079	1.47 (0.55–3.94)	0.4421
Random blood glucose ≥ 7.8mmol/l	1.13 (0.54–2.34)	0.7459	1.09 (0.51–2.33)	0.8225
Increased waist circumference*	2.95 (1.79–4.87)	0.0001	2.49 (1.39–4.43)	0.0020
ART regimen				
No ART	Ref	Ref	Ref	Ref
TDF-based	1.18 (0.88–1.58)	0.2794	1.10 (0.81–1.49)	0.5506
AZT-based	1.40 (1.07–1.84)	0.0152	1.26 (0.95–1.68)	0.1090
D4T-based	1.42 (0.97–2.06)	0.068	1.22 (0.82–1.81)	0.3226
LPV-based	0.91 (0.41–2.03)	0.8212	0.97 (0.42–2.25)	0.9385
CD4 count (cells/mm³)				
Missing	0.71 (0.53–0.94)	0.0165	0.72 (0.54–0.97)	0.0307
0–100	0.47 (0.23–0.92)	0.0287	0.49 (0.24–0.99)	0.0472
101–200	0.78 (0.47–1.29)	0.3369	0.67 (0.40–1.14)	0.1406
201–350	0.67 (0.50–0.91)	0.0112	0.59 (0.43–0.82)	0.0015
351–500	0.84 (0.62–1.12)	0.2315	0.77 (0.56–1.04)	0.0882
> 500	Ref	Ref	Ref	Ref

*Females ≥ 90 cm, males ≥ 100 cm.

Table 4. Unadjusted and adjusted odds ratios for elevated total cholesterol

	Unadjusted OR		*Adjusted OR*	
Characteristic	*OR (95% CI)*	p-*value*	*OR (95% CI)*	p-*value*
Male gender	0.85 (0.61–1.17)	0.3194	0.83 (0.59–1.17)	0.2806
Age ≥ 40 years	2.21 (1.63–3.00)	0.0001	1.95 (1.42–2.69)	0.0001
Smoker	0.22 (0.03–1.64)	0.1404	0.22 (0.03–1.67)	0.1434
BMI ≥ 30 kg/m²	2.15 (0.95–4.86)	0.0647	1.03 (0.39–2.74)	0.946
Random blood glucose ≥ 7.8 mmol/l	1.96 (0.83–4.62)	0.1252	1.99 (0.82–4.81)	0.1278
Increased waist circumference*	2.68 (1.64–4.36)	0.0001	2.06 (1.14–3.71)	0.0164
ART regimen				
No ART	Ref	Ref	Ref	Ref
TDF-based	2.47 (1.45–4.22)	0.0009	2.20 (1.28–3.78)	0.0042
AZT-based	2.84 (1.72–4.71)	0.0001	2.50 (1.50–4.18)	0.0004
D4T-based	3.86 (2.14–6.95)	0.0001	3.13 (1.72–5.71)	0.0002
LPV-based	1.98 (0.55–7.17)	0.2968	1.85 (0.50–6.80)	0.3536
CD4 count (cells/mm³)				
Missing	0.74 (0.49–1.11)	0.147	0.87 (0.57–1.33)	0.5217
0–100	1.04 (0.42–2.60)	0.9306	1.13 (0.44–2.92)	0.7964
101–200	0.48 (0.20–1.16)	0.1029	0.46 (0.19–1.13)	0.0885
201–350	0.79 (0.51–1.22)	0.2884	0.79 (0.50–1.25)	0.3174
351–500	0.93 (0.62–1.39)	0.7106	0.92 (0.60–1.41)	0.6951
> 500	Ref	Ref	Ref	Ref

*Females ≥ 90 cm, males ≥ 100 cm.

OR 2.06 (1.14–3.71), $p = 0.0164$] were associated with having a raised total cholesterol level. In addition, raised total cholesterol was more likely in those on TDF [adjusted OR 2.20 (1.28–3.78), $p = 0.0042$], AZT [adjusted OR 2.50 (1.50–4.18), $p = 0.004$] and D4T-containing regimens [adjusted OR 3.13 (1.72–5.71), $p = 0.002$]. However, the median duration on ART was not significantly different for those with or without a raised total cholesterol level (Mann–Whitney test, $p = 0.1261$). There was no significant association between CD4 count and total cholesterol level (Table 4).

Thirty-one (2.1%) subjects had a random blood glucose level of > 7.8 mmol/l. These patients were referred to the physician for fasting glucose determination and/or oral glucose tolerance tests.

Eight (0.55%) of those above 40 years of age had more than 10% risk of developing a major adverse cardiovascular event in 10 years, according the WHO (Afri-E) risk score performed on these clients.

Discussion

In this study, cardiovascular screening of people living with HIV revealed a significant prevalence of undiagnosed hypertension (13.3%) and raised total cholesterol levels (14%), two of the major cardiovascular risk factors. Possible aetiological factors for hypertension include traditional risk factors (such as age, gender, smoking and obesity), ART, or possibly HIV infection itself. Our analysis of risk factors indicated significant associations between the occurrence of hypertension and male gender, older age (> 40 years) and increased waist circumference. There was however no association between ART regimen and hypertension, suggesting that other factors may have been contributory.

In a population survey targeting a peri-urban community in Nairobi, prevalence of hypertension was 22%,[12] which is higher than seen in this study. One of the possible reasons for this disparity is that despite living with HIV, the age of this cohort was relatively young and with fewer smokers compared to those reported in the general population (2015 Kenya STEPS survey). Also, the prevalence of other known risk factors for hypertension such as overweight and obesity was at 14%, well lower than reported in the national STEPS survey (27%).

In another retrospective review of data from an HIV-positive population in western Kenya, the prevalence of hypertension was 11.2% in men and 7.4% in women.[13] The figures observed in this review compare well with those found in our study.

Possible aetiological factors for high cholesterol levels include genetic factors, diet, ART or HIV infection itself. After adjusting for confounders, elevated cholesterol level was associated with three ART regimens (TDF, AZT and D4T) suggesting a potential causal relationship. However, since a full lipid profile was not performed, it remains unclear if this was due to a raised low-density lipoprotein cholesterol level.

A study in Tanzania showed a high prevalence of dyslipidaemia (low high-density lipoprotein cholesterol and elevated triglyceride levels) in an ART-naïve cohort of HIV patients.[5] There is therefore a need for further research to illustrate the role of ART therapy on the patterns of dyslipidaemia.

The prevalence of smoking, obesity, glucose intolerance and diabetes were low in this population at 1.9, 12.1 and 2.6%, respectively, and only 0.6% had a WHO cardiovascular risk score > 10%. This is much lower compared to the peri-urban population study of Nairobi where 10% were smokers, 5% had diabetes, and more than 40% had central obesity.[12] Our rural hospital setting may present a different HIV population where disease and lifestyle advice provided to the patients may have altered risk factors, particularly smoking incidence.

With increasing longevity of people living with HIV, the prevalence of hypertension, hyperlipidaemia and glucose intolerance is likely to increase. Therefore routine and systematic screening for cardiovascular risk factors among this population is crucial. The majority of cardiovascular risk factors, also seen in people with HIV, such as smoking, hypertension and obesity, are modifiable, therefore early identification and treatment of these conditions provides an opportunity to improve the quality of care and possibly survival rate in this population. Existing studies conducted in sub-Saharan Africa suggest there is little knowledge of the risk posed by CVD in this population.[14] There is therefore a need to establish CVD care in HIV programmes to potentially mitigate adverse cardiovascular events in these patients.[15]

This study has several limitations, including collecting data from patient charts at one time point. Further studies are needed to establish how screening, referral and evidence-based interventions could reduce cardiovascular risk of people living with HIV in rural Kenya and beyond. Cardiovascular risk was determined after a median duration of 32 months of ART. A longer period of observation may be required to detect transition in cardiovascular risk. However the high prevalence of hypertension indicates that there was a considerable amount of undiagnosed incipient and actual hypertension in this population. Lastly, fasting lipid profiles were not performed where elevated non-fasting values were found, and inferences from an elevated total cholesterol level may not accurately reflect the prevalence of hypercholesterolaemia. However, recent guidelines advocate the use of non-fasting cholesterol tests.[16] Our data are from 2013 to 2016, and the situation in terms of ART regimens and cardiovascular risk may have changed since then.

Conclusion

CVD screening in a primary HIV-care clinic revealed a high prevalence of undiagnosed hypertension and raised total cholesterol levels, and suggests an association between raised total cholesterol level and nucleoside reverse-transcriptase inhibitor (NRTI)-based ART regimens in an HIV-infected African population. Our findings provide further rationale for integrating routine cardiovascular risk-factor screening into HIV-care services in resource-limited settings. Larger studies with more detailed investigations and longer follow up are recommended.

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