Cardiovascular risk factors and markers of myocardial injury and inflammation in people living with HIV in Nairobi, Kenya: a pilot cross-sectional study

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ABSTRACT

Objectives To determine the prevalence of cardiovascular disease (CVD) risk factors and explore associations with high-sensitivity cardiac troponin I (hsTnI) and high-sensitivity C-reactive protein (hsCRP) in people living with HIV (PLHIV) in Kenya.

Design Pilot cross-sectional study.

Setting Data were collected from community HIV clinics across two sites in Nairobi, Kenya, from July 2019 to May 2020.

Participants Convenience sample of 200 PLHIV (≥30 years with no prior history of CVD).

Outcome measures Prevalence of cardiovascular risk factors and its association with hsTnI and hsCRP levels.

Results Across 200 PLHIV (median age 46 years, IQR 38–53; 61% women), the prevalence of hypercholesterolaemia (total cholesterol >6.1 mmol/L) and hypertension were 19% (n=30/199) and 30% (n=60/200), respectively. Smoking and diabetes prevalence was 3% (n=5/200) and 4% (n=7/200). HscTnI was below the limit of quantification (<2.5 μg/L) in 38% (n=75/198), high (≥3 μg/L), intermediate (1–3 μg/L) and low (<1 μg/L) hsCRP levels were found in 38% (n=75/198), 33% (n=65/198) and 29% (n=58/198), respectively. Framingham laboratory-based risk scores classified 83% of PLHIV at low risk with 12% and 5% at intermediate and high risk, respectively. Older age (adjusted OR (aOR) per year increase 1.05, 95% CI 1.01 to 1.08) and systolic blood pressure (140–159 mm Hg (aOR 2.96; 95% CI 1.09 to 7.90) and >160 mm Hg (aOR 4.68, 95% CI 1.55 to 14) compared with <140 mm Hg) were associated with hscTnI levels. No associations were observed between hsCRP and CVD risk factors.

Conclusion The majority of PLHIV—using traditional risk estimation systems—have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. Hypertension and hypercholesterolaemia were common while smoking and diabetes rates remained low. While hscTnI values were associated with increasing age and raised blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Involvement of people living with HIV from a low-income and middle-income settings and from distinct socioeconomic backgrounds.
⇒ Assessment of relatively novel biochemical markers of cardiovascular risk alongside more traditional cardiovascular risk factors.
⇒ Due to the cross-sectional design, we were unable to evaluate the associations between novel biochemical markers and future cardiovascular events.
⇒ The study population was from an urban setting, so generalisability to rural settings is limited.
⇒ There was no age-matched and sex-matched uninfected control group.

INTRODUCTION

More than 35 million people are infected with the HIV with two-thirds being resident in sub-Saharan Africa. Although the global incidence for HIV has stabilised, the wide availability of combined antiretroviral therapy (ART) has dramatically improved survival, resulting in a steady increase in prevalence over the last two decades. Despite this improvement in survival has been primarily attributed to a reduction in opportunistic infections especially in low-income and lower-middle-income nations. Conversely, mortality due to non-communicable illnesses especially cardiovascular disease (CVD) has been rising and now account for the majority of deaths in people living with HIV (PLHIV). PLHIV-based on studies in high-income countries—have a higher risk of CVD. Despite this higher risk, previous studies have indicated that PLHIV in sub-Saharan Africa have a lower prevalence of traditional cardiovascular risk factors in comparison to uninfected individuals. Strategies to risk stratify and mitigate CVD in this population is now urgently required but is challenging in resource limited nations and it remains
unclear on optimal approaches with recommendations differing across regions globally.\(^{12}\)

In this cross-sectional pilot study of PLHIV in Kenya, we evaluate the prevalence of traditional cardiovascular risk factors and the distribution of estimated cardiovascular risk using traditional risk scores. We further explore the distribution of markers of myocardial injury and inflammation in this population. Our additional objectives are to evaluate the logistic feasibility, including recruitment rates, for a full-scale study investigating mechanisms in HIV-associated CVD.

**METHODS**

**Study setting and population**

This was a pilot, prospective, cross-sectional study of PLHIV ≥30 years in Nairobi, Kenya. Population sample size was determined based on the fixed recruitment period from July 2019 to May 2020. Patients were recruited based on convenient sampling and invited to participate as long as they received care at the two clinical sites (Aga Khan University Hospital and Coptic Hope Center for Infectious Diseases) where the researchers and their research teams were based. Aga Khan University Hospital is a fee-for-service tertiary care centre generally serving a more affluent population while the Coptic Hope Center for Infectious Diseases is a Centre of Disease Control President’s Emergency Plan For AIDS Relief funded institution to provide free ART to Kenyans who are unable to afford HIV care and treatment.\(^{13}\) Participants with known CVD (previous myocardial infarction or stroke) were excluded.

**Study procedures and blood sampling**

All participants completed a standardised questionnaire to capture data on demographics, including self-reported cardiovascular risk factors, medical history, current medication and HIV factors including time since diagnosis. Data were captured on handheld devices electronically. Anthropometric and haemodynamic data including office blood pressure, height, weight and heart rate were captured.

**Blood sampling**

Blood samples were obtained from participants through standard venepuncture. Basic clinical chemistry and haematology was performed. This included assessment of renal function, glycaemic control, non-fasted lipid profiles, high-sensitivity cardiac troponin I (hsTnI) and high-sensitivity C-reactive protein (hsCRP). Given laboratory constraints, haemoglobin A1c (HbA1c) and haematology was only measured in the Aga Khan University Hospital population.

**High-sensitivity troponin I**

The Siemens Atellica IM High Sensitivity Troponin I assay (Siemens Healthineers) is a three-site sandwich immunoassay with a limit of detection of 1.6 ng/L and limit of quantification of 2.5 ng/L. The upper reference limit 99th centile was determined in 2007 samples from healthy individuals as 34 ng/L in women, and 53 ng/L in men, with a single threshold of 45 ng/L. In the reference range population, 75% of patients had values greater than the limit of detection. The level where the interassay coefficient of variation is <10% is 6 ng/L.\(^{14}\)

**HsCRP**

The Siemens Atellica hsCRP assay was used to measure hsCRP levels in stored serum. The assay range is from 0.1 to 50 mg/L with a coefficient of variation of 6.8% at 1.16 mg/L.\(^{15}\)

**Study definitions**

Traditional cardiovascular risk factors were defined as those routinely measured in cardiovascular risk estimation systems and include basic anthropometry, diabetes and smoking status, lipid profile and arterial blood pressure assessment. Body mass index was calculated from measured height and weight and classified as normal weight (18.5–24.9 kg/m\(^2\)), overweight (25.0–29.9 kg/m\(^2\)) and obese (equal to or greater than 30.0 kg/m\(^2\)). Current or past smoking history was self-reported by participants. Hypertension was defined as self-reported hypertension or measured systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg, or physician-prescribed blood pressure-lowering medications.\(^{16}\) Dyslipidaemia was defined as a self-reported history. Hypercholesterolaemia was defined as a total cholesterol ≥2.61 mmol/L. A high low-density lipoprotein (LDL) was defined as levels >4.1 mmol/L.\(^{17}\) Diabetes mellitus was defined as self-reported type 1 or 2 diabetes mellitus. Patients, in whom HbA1c was measured, were classified as those with high (≥6.5%), intermediate (5.7%–6.4%) and low levels (<5.7%).\(^{18}\) The hsCRP was categorised as low (<1 mg/L), intermediate (1–3 mg/L) or high (>3 mg/L).\(^{19}\) HsTnI levels were categorised as below the limit of quantification (2.5 ng/L), above the limit of quantification but below the 99th centile upper reference limit and above the 99th centile upper reference limit (45 ng/L).\(^{20}\)

**Statistical analysis**

Baseline demographics, clinical and lifestyle variables, laboratory biomarkers including markers of myocardial injury, inflammation, glycaemic control and lipid profiles were summarised overall and stratified by gender. Continuous variables were reported as median and IQR, while the categorical variables were summarised as frequencies and percentages. Statistical differences between groups were assessed using Pearson’s \(\chi^2\) test or Fisher’s exact test and unpaired two-samples Wilcoxon test or Student’s \(t\)-test as indicated. Sex-specific Framingham laboratory-based risk equations were used to quantify the estimated 10-year CVD risk for each study participant. The equation used age, gender, smoking status, use of anti-hypertensive medications, prevalent diabetes and SBP.
### Table 1  Baseline demographics and clinical characteristics*

| Characteristics                                      | All patients (n=200) | Sex                   | Females (n=121) | Males (n=79) | P value† |
|------------------------------------------------------|----------------------|-----------------------|-----------------|--------------|----------|
| Age, median (Q1, Q3), years                          | 45.5 (37.7, 52.6)    | 44.2 (37.3, 50.5)     | 47.3 (38.0, 53.1)| 0.206        |
| Years of education, median (Q1, Q3)                  | 14.0 (12.0, 16.0)    | 14.0 (12.0, 16.0)     | 15.0 (12.0, 16.5)| 0.174        |
| Highest level of education attained                  |                      |                       |                 |              |
| Primary/none/do not know, %                          | 30/200 (15.0)        | 18/121 (14.9)         | 12/79 (15.2)    | 0.825        |
| Secondary, %                                         | 45/200 (22.5)        | 29/121 (24.0)         | 16/79 (20.3)    |              |
| Higher education/university, %                       | 125/200 (62.5)       | 74/121 (61.2)         | 51/79 (64.6)    |              |
| Marital status                                       |                      |                       |                 |              |
| Married (monogamous/polygamous), %                   | 128/200 (64.0)       | 64/121 (52.9)         | 64/79 (81.0)    | <0.001       |
| Single                                               | 26/200 (13.0)        | 23/121 (19.0)         | 3/79 (3.8)      |              |
| Separated/widowed/divorced/refused/cohabiting/others, %| 46/200 (23.0)        | 34/121 (28.1)         | 12/79 (15.2)    |              |
| Employment status                                    |                      |                       |                 |              |
| Salaried Job or self-employed, %                     | 180/200 (90.0)       | 105/121 (86.8)        | 75/79 (94.9)    | 0.148        |
| Unemployed/housewife/retiree, %                      | 13/200 (6.5)         | 11/121 (9.1)          | 2/79 (2.5)      |              |
| Casual labourer, %                                   | 7/200 (3.5)          | 5/121 (4.1)           | 2/79 (2.5)      |              |
| Household income per month                           |                      |                       |                 |              |
| <15001 KES, %                                        | 34/198 (17.2)        | 26/119 (21.8)         | 8/79 (10.1)     | 0.051        |
| >15001 KES, %                                        | 164/198 (82.8)       | 93/119 (78.2)         | 71/79 (89.9)    |              |
| Cardiovascular risk factors                          |                      |                       |                 |              |
| Smoking                                              |                      |                       |                 |              |
| Current smoker, %                                    | 5/200 (2.5)          | 2/121 (1.7)           | 3/79 (3.8)      | <0.001       |
| Ex-smoker, %                                         | 44/200 (22.0)        | 11/121 (9.1)          | 33/79 (41.8)    |              |
| Never smoker, %                                      | 151/200 (75.5)       | 108/121 (89.3)        | 43/79 (54.4)    |              |
| Diabetes, %                                          | 7/200 (3.5)          | 4/121 (3.3)           | 3/79 (3.8)      | 0.661        |
| Self-reported hypertension,‡ %                       | 44/200 (22.0)        | 30/121 (24.8)         | 14/79 (17.7)    | 0.315        |
| Cumulative hypertension,§ %                          | 60/200 (30.0)        | 34/121 (28.1)         | 26/79 (32.9)    | 0.570        |
| Self-reported dyslipidaemia, %                       | 1/197 (0.5)          | 1/119 (0.8)           | 0/78 (0.0)      | 0.153        |
| Chronic kidney disease, %                            | 2/200 (1.0)          | 1/121 (0.8)           | 1/79 (1.3)      | 0.863        |
| HIV                                                  |                      |                       |                 |              |
| Time since (months) HIV infection, median (Q1, Q3)   | 143.0 (59.0, 191.0)  | 144.0 (62.0, 191.0)   | 131.0 (56.5, 191.0) | 0.574 |
| Currently on ART, %                                  | 195/200 (97.5)       | 119/121 (98.3)        | 76/79 (96.2)    | 0.385        |
| Medical history                                      |                      |                       |                 |              |
| Malaria, %                                           | 21/200 (10.5)        | 10/121 (8.3)          | 11/79 (13.9)    | 0.298        |
| Tuberculosis, %                                      | 12/200 (6.0)         | 7/121 (5.8)           | 5/79 (6.3)      | 1.000        |
| Clinical characteristics                             |                      |                       |                 |              |
| Body mass index, BMI (Kg/m²), median (Q1, Q3)        | 26.8 (23.4, 30.8)    | 27.9 (23.8, 32.3)     | 26.0 (23.2, 29.6) | 0.010 |
| BMI <25, %                                           | 71/200 (35.5)        | 37/121 (30.6)         | 34/79 (43.0)    | 0.100        |
| BMI 25–29, %                                         | 71/200 (35.5)        | 43/121 (35.5)         | 41/79 (33.9)    |              |
| BMI >30, %                                           | 58/200 (29.0)        | 41/121 (33.9)         | 17/79 (21.5)    |              |
| Systolic blood pressure (mm Hg), median (Q1, Q3), n=200 | 120.0 (110.0, 133.0) | 120.0 (110.0, 130.0)  | 122.0 (111.5, 133.0) | 0.272 |

Continued
The risk estimations were computed according to algorithms accessed at https://framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/. Predicted cardiovascular event risk percentage over the next 10 years was classified as low (<10%), intermediate (10%–20%) and high risk (>20%).

In further analysis, we evaluated the relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors. We calculated the 25th and 75th percentiles of observed hsTnI data and ordinally scaled it as <2.50 ng/L (undetectable), 2.50–3.02 ng/L, 3.02–7.12 ng/L, ≥7.12 ng/L given the skewness of the variable. Three multivariable ordinal (cumulative logit) models and linear regression models with hsTnI and hsCRP as the response variable, respectively, were fitted. The independent variables were age, sex and cardiovascular risk factors. Model I adjusted for age per year increase, sex, study site as a surrogate for socioeconomic status and creatinine. Model II additionally adjusted for hypertension, diabetes and smoking status (never smoker, former smoker, current smoker). Model III adjusted for variables in Model I plus SBP (SBP <130 mm Hg, SBP 130–139 mm Hg, SBP 140–159 mm Hg, SBP >160 mm Hg) and hsCRP or hsTnI. Models were constructed on complete cases with no imputation. All analysis was carried out in R (V.4.1.2).

Patients were enrolled only after providing written informed consent prior to participation. Site approval was obtained from the Coptic Hope Center for Infectious Diseases in Nairobi. The research was carried out in accordance with the Helsinki Declaration’s principles.

Patient and public involvement
No patient involvement.

RESULTS
Two hundred patients (median age 46 years (IQR 38–53 years), 61% women) were recruited in this cross-sectional study consisting (online supplementary figure S1). Prevalence of smoking was 2.5% across the cohort and higher in men compared with women. Hypertension was the most common cardiovascular risk factor at 30% with rates higher in men (33%) compared with women (28%). Self-reported dyslipidaemia was low at 0.5% but much higher when classified according to a total cholesterol concentration ≥6.1 mmol/L (19%). The prevalence of elevated LDL ≥4.2 mmol/L was 14%. Seventeen per cent of the

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**Table 1** Continued

| Characteristics | All patients (n=200) | Sex                                      | P value† |
|-----------------|---------------------|------------------------------------------|----------|
|                 |                     | Females (n=121)                        | Males (n=79) |       |
| SBP <130 mm Hg, % | 136/200 (68.0)     | 86/121 (71.1)                          | 50/79 (63.3) | 0.173   |
| SBP 130–139 mm Hg, % | 30/200 (15.0)    | 19/121 (15.7)                          | 11/79 (13.9) |         |
| SBP 140–159 mm Hg, % | 19/200 (9.5)     | 7/121 (5.8)                            | 12/79 (15.2) |         |
| SBP >160 mm Hg, % | 15/200 (7.5)       | 9/121 (7.4)                            | 6/79 (7.6)   |         |
| Diastolic blood pressure (mm Hg), median (Q1, Q3), n=200 | 78.0 (71.0, 85.0) | 77.0 (71.0, 84.0) | 80.0 (72.0, 85.0) | 0.301   |
| DBP <85 mm Hg, % | 149/200 (74.5)    | 92/121 (76.0)                          | 57/79 (72.2) | 0.417   |
| DBP 85–89 mm Hg, % | 22/200 (11.0)     | 10/121 (8.3)                           | 12/79 (15.2) |         |
| DBP 90–99, %     | 17/200 (8.5)      | 12/121 (9.9)                           | 5/79 (6.3)   |         |
| DBP >100, %      | 12/200 (6.0)      | 7/121 (5.8)                            | 5/79 (6.3)   |         |
| Heart rate (bpm) median (Q1, Q3) | 78.0 (74.0, 82.0) | 76.5 (74.8, 84.2) | 78.0 (72.0, 81.0) | 0.474   |

Current cardiovascular medications

| RAAS modulators, % | 16/200 (8.0) | 11/121 (9.1) | 5/79 (6.3) | 0.662   |
| Calcium channel blockers, % | 8/200 (4.0) | 5/121 (4.1) | 3/79 (3.8) | 1.000   |
| Beta-blockers, %   | 8/200 (4.0) | 5/121 (4.1) | 3/79 (3.8) | 1.000   |
| Diuretics, %       | 10/200 (5.0) | 8/121 (6.6) | 2/79 (2.5) | 0.321   |
| Statins, %         | 2/200 (1.0) | 1/121 (0.8) | 1/79 (1.3) | 1.000   |

*Number of patients may not sum to the corresponding column totals where there are missing data for the variable.
†P value from χ² test or Fisher’s exact test for categorical variables and unpaired two-sample Wilcoxon test for continuous variables, two-sided; bold p values indicate statistical significance (p<0.05).
‡Self-reported physician-diagnosed hypertension.
§Self-reported hypertension or measured systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg, or physician-prescribed blood pressure-lowering medications.

ART, antiretroviral therapy; HDL, high density lipoprotein; KES, Kenya shillings currency code; RAAS, Renin–angiotensin–aldosterone system.
The population had a SBP ≥140 mm Hg and 15% of the population had a DBP ≥90 mm Hg. Obesity rates were high with 29% considered obese and 36% overweight. Obesity rates were higher in women at 34% compared with men (22%). Prior history of malaria and tuberculosis remained high at 11% and 6%, respectively. Over 90% of participants were receiving ART and median duration of diagnosis to study recruitment was 12 years (tables 1 and 2). Given differences in the population served at Aga Khan University and Coptic hospitals, we observed important differences in baseline characteristics. Patient treated at Coptic hospital has lower income levels and higher rates of elevated blood pressure (online supplemental table S1).

**Table 2  Biochemistry and haematology**

| Characteristics            | All patients (n=200) | Sex                                  | Females (n=121) | Males (n=79) | P value† |
|----------------------------|----------------------|--------------------------------------|-----------------|--------------|----------|
| Creatinine, median (Q1, Q3), n=197 | 85.0 (73.0, 101.0) | 77.5 (69.0, 89.3) | 99.0 (89.0, 113.0) | <0.001 |
| Urea, median (Q1, Q3), n=196   | 3.7 (3.1, 4.6)     | 3.6 (3.0, 4.3)     | 3.8 (3.2, 5.0)     | 0.013 |
| Haemoglobin, mean (SD), n=98‡  | 14.01 (2.06)       | 12.90 (1.77)       | 15.31 (1.55)       | <0.001 |
| Glucose, median (Q1, Q3), n=197 | 4.8 (4.4, 5.3)     | 4.8 (4.3, 5.5)     | 4.9 (4.5, 5.3)     | 0.169 |
| HbA1c, median (Q1, Q3), n=98‡  | 5.6 (5.4, 5.9)     | 5.6 (5.4, 5.8)     | 5.8 (5.4, 6.1)     | 0.013 |
| HbA1c <5.7, %                 | 50/98 (51.0)       | 34/53 (64.2)       | 16/45 (35.6)       | 0.004 |
| HbA1c 5.7–6.4, %              | 45/98 (45.9)       | 19/53 (35.8)       | 26/45 (57.8)       |          |
| HbA1c ≥6.5, %                 | 3/98 (3.1)         | 0/53 (0.0)         | 3/45 (6.7)         |          |

**Lipid profiles**

| Characteristics            | All patients (n=196) | Sex                                  | Females (n=121) | Males (n=79) | P value† |
|----------------------------|----------------------|--------------------------------------|-----------------|--------------|----------|
| Total cholesterol, median (Q1, Q3), n=196 | 4.6 (3.9, 5.1)     | 4.7 (3.9, 5.2)     | 4.5 (3.9, 5.1)     | 0.706 |
| TC <4.7, %                  | 107/196 (54.6)      | 59/118 (50.0)       | 48/78 (61.5)       | 0.393 |
| TC 4.8–5.1, %               | 22/196 (11.2)       | 15/118 (12.7)       | 7/78 (9.0)         |          |
| TC 5.2–6.1, %               | 30/196 (15.3)       | 21/118 (17.8)       | 9/78 (11.5)        |          |
| TC ≥6.2, %                  | 37/196 (18.9)       | 23/118 (19.5)       | 14/78 (17.9)       |          |
| LDL, median (Q1, Q3), n=196 | 3.0 (2.3, 3.6)     | 3.0 (2.4, 3.7)     | 3.0 (2.3, 3.5)     | 0.747 |
| LDL <2.6                    | 75/196 (38.3)       | 46/118 (39.0)       | 29/78 (37.2)       | 0.619 |
| LDL 2.6–3.3                 | 53/196 (27.0)       | 30/118 (25.4)       | 23/78 (29.5)       |          |
| LDL 3.4–4.1                 | 41/196 (20.9)       | 23/118 (19.5)       | 18/78 (23.1)       |          |
| LDL ≥4.2                    | 27/196 (13.8)       | 19/118 (16.1)       | 8/78 (10.3)        |          |
| HDL, median (Q1, Q3), n=196 | 1.2 (1.0, 1.5)      | 1.2 (1.1, 1.5)      | 1.1 (1.0, 1.3)     | 0.001 |
| Triglycerides, median (Q1, Q3), n=196 | 1.4 (0.9, 2.0)     | 1.2 (0.9, 1.7)     | 1.7 (1.0, 2.7)     | 0.0005 |
| Trig <1.7                   | 123/196 (62.8)      | 86/118 (72.9)       | 37/78 (47.4)       | <0.0001 |
| Trig 1.7–2.2                | 32/196 (16.3)       | 19/118 (16.1)       | 13/78 (16.7)       |          |
| Trig ≥2.3                   | 41/196 (20.9)       | 13/118 (11.0)       | 28/78 (35.9)       |          |

**Cardiac and inflammatory biomarkers**

| Characteristics            | All patients (n=169) | Sex                                  | Females (n=103) | Males (n=66) | P value† |
|----------------------------|----------------------|--------------------------------------|-----------------|--------------|----------|
| High sensitivity troponin I, median (Q1, Q3), n=169 | 2.5 (2.5, 3.0)     | 2.5 (2.5, 2.5)     | 2.7 (2.5, 3.8)     | <0.0001 |
| hscTnI <2.5 ng/L, %         | 109/169 (64.5)       | 78/103 (75.7)     | 31/66 (47.0)       | <0.001 |
| hscTnI 2.5–45 ng/L          | 59/169 (34.9)       | 24/103 (23.3)     | 35/66 (53.0)       |          |
| hscTnI ≥45 ng/L             | 1/169 (0.6)         | 1/103 (1.0)       | 0/66 (0.0)         |          |
| High-sensitivity CRP, median (Q1, Q3), n=198 | 2.0 (0.8, 4.2)     | 2.2 (0.9, 4.5)     | 1.5 (0.8, 3.8)     | 0.144 |
| hsCRP <1 mg/L               | 58/198 (29.3)       | 31/120 (25.8)     | 27/78 (34.6)       | 0.300 |
| hsCRP 1–3 mg/L              | 65/198 (32.8)       | 39/120 (32.5)     | 26/78 (33.3)       |          |
| hsCRP >3 mg/L               | 75/198 (37.9)       | 50/120 (41.7)     | 25/78 (32.1)       |          |

*Number of patients may not sum to the corresponding column totals where there are missing data for the laboratory marker.†P value from χ² test or Fisher’s exact test for categorical variables and unpaired two-sample Wilcoxon test or Student’s t-test for continuous variables, two-sided; bold p values indicate statistical significance (p<0.05).
‡Haemoglobin and haemoglobin A1c (HbA1c) summaries are from Aga Khan University Hospital only.
hsCRP, high-sensitivity C-reactive protein; hscTnI, high-sensitivity cardiac troponin I; LDL, low-density lipoprotein.
### Table 3  Cardiovascular risk factors, markers of myocardial injury and inflammation by cardiovascular risk category

| Variable                      | Framingham risk score classification (lipid)† | P value for trend‡ |  |
|-------------------------------|-----------------------------------------------|--------------------|---|
|                               | Low (Framingham risk score classification)    | Increasing         | Two-sided |  |
|                               | Intermediate (lipid)                          |                     |           |  |
|                               | High (lipid)                                  |                     |           |  |
| **Males**                     |                                               |                     |           |  |
| All (%)                       | 58 (73.4)                                     | 14 (17.7)           | 7 (8.9)   |  |
| Smoking                       |                                               |                     |           |  |
| Current smoker, %             | 3/58 (5.2)                                    | 0/14 (0.0)          | 0/7 (0.0) |  |
| Ex-smoker, %                  | 22/58 (37.9)                                  | 6/14 (42.9)         | 5/7 (71.4)|  |
| Never smoker, %               | 33/58 (56.9)                                  | 8/14 (57.1)         | 2/7 (28.6)|  |
| Diabetes, %                   | 3/58 (5.2)                                    | 0/14 (0.0)          | 0/7 (0.0) |  |
| Hypertension, %               | 12/58 (20.7)                                  | 6/14 (42.9)         | 7/7 (100.0)|<0.001|<0.001|
| Hyperlipidaemia, %            | 0/58 (0.0)                                    | 0/13 (0.0)          | 0/7 (0.0) | – | – |
| **Lipid profiles**            |                                               |                     |           |  |
| Total cholesterol, median (Q1, Q3) | 4.3 (3.8, 4.9) | 4.5 (4.3, 5.4) | 6.2 (5.0, 6.8) | 0.005|0.007|
| TC <4.7, %                    | 39/57 (68.4)                                  | 8/14 (57.1)         | 1/7 (14.3)| – | <0.001|
| TC 4.8–5.1, %                 | 7/57 (12.3)                                   | 0/14 (0.0)          | 0/7 (0.0) | – | – |
| TC 5.2–6.1, %                 | 5/57 (8.8)                                    | 4/14 (28.6)         | 0/7 (0.0) | – | – |
| TC ≥6.2, %                    | 6/57 (10.5)                                   | 2/14 (14.3)         | 6/7 (85.7) | – | – |
| LDL, median (Q1, Q3)          | 3.0 (2.3, 3.4)                                | 3.2 (2.3, 3.5)      | 3.9 (3.5, 5.2) | 0.016|0.039|
| **Cardiac and inflammatory biomarkers** |                                               |                     |           |  |
| High sensitivity troponin I, median (Q1, Q3) | 2.5 (2.5, 3.4) | 3.4 (2.8, 5.2) | 4.1 (2.9, 7.1) | 0.013|0.020|
| hsTnI <2.5 ng/L, %            | 26/48 (54.2)                                  | 3/11 (27.3)         | 2/7 (28.6) | – | 0.083|
| hsTnI 2.5–45 ng/L             | 22/48 (45.8)                                  | 8/11 (72.7)         | 5/7 (71.4) | – | – |
| hsTnI ≥45 ng/L                | 0/48 (0.0)                                    | 0/11 (0.0)          | 0/7 (0.0) | – | – |
| High-sensitivity CRP, median (Q1, Q3) | 1.5 (0.8, 4.0) | 2.3 (0.8, 3.1) | 1.0 (0.7, 3.6) | 0.523|0.95|
| hsCRP <1 mg/L                 | 19/57 (33.3)                                  | 5/14 (35.7)         | 3/7 (42.9) | – | 0.782|
| hsCRP 1–3 mg/L                | 20/57 (35.1)                                  | 41/4 (28.6)         | 2/7 (28.6) | – | – |
| hsCRP ≥3 mg/L                 | 18/57 (31.6)                                  | 51/4 (35.7)         | 2/7 (28.6) | – | – |
| Creatinine, median (Q1, Q3)   | 100.0 (89.5, 113.2)                           | 98.5 (94.8, 115.0)  | 91.0 (79.0, 104.5) | 0.702|0.610|
| **Females**                   |                                               |                     |           |  |
| All (%)                       | 108 (89.3)                                    | 9 (7.4)             | 4 (3.3)   | – | 0.241|
| Smoking                       |                                               |                     |           |  |
| Current smoker, %             | 2/108 (1.9)                                   | 0/9 (0.0)           | 0/4 (0.0) | – | 0.241|
| Ex-smoker, %                  | 11/108 (10.2)                                 | 0/9 (0.0)           | 0/4 (0.0) | – | – |
| Never smoker, %               | 95/108 (88.0)                                 | 9/9 (100.0)         | 4/4 (100.0) | – | – |
| Diabetes, %                   | 0/108 (0.0)                                   | 2/9 (22.2)          | 2/4 (50.0) | 1.000|<0.0001|
| Hypertension, %               | 24/108 (22.2)                                 | 7/9 (77.8)          | 3/4 (75.0) | <0.0001|<0.001|
| Hyperlipidaemia, %            | 0/106 (0.0)                                   | 1/9 (11.1)          | 0/4 (0.0) | 0.976|0.048|
| **Lipid profiles**            |                                               |                     |           |  |
| Total cholesterol, median (Q1, Q3) | 4.6 (3.8, 5.1) | 5.4 (4.9, 6.1) | 4.4 (4.3, 4.7) | 0.07|0.031|
| TC <4.7, %                    | 54/105 (51.4)                                 | 2/9 (22.2)          | 3/4 (75.0) | – | 0.883|
| TC 4.8–5.1, %                 | 13/105 (12.4)                                 | 2/9 (22.2)          | 0/4 (0.0) | – | – |
| TC 5.2–6.1, %                 | 18/105 (17.1)                                 | 2/9 (22.2)          | 1/4 (25.0) | – | – |
| TC ≥6.2, %                    | 20/105 (19.0)                                 | 3/9 (33.3)          | 0/4 (0.0) | – | – |
| LDL, median (Q1, Q3)          | 2.9 (2.4, 3.5)                                | 4.0 (3.3, 4.2)      | 2.9 (2.6, 3.2) | 0.042|0.082|

Continued
Stored serum was available to measure hscTnI concentrations in 169 of the 200 participants. Despite using a hscTnI assay, the majority had concentrations below the limit of quantification at ≤2.5 ng/L (n=109/169, 65%). Fifty-nine patients (n=59/169, 35%) had concentration levels above the limit of quantification but below the 99th centile upper reference limit. Serum hsCRP was measured in 198 of the 200 participants. The median hsCRP was 2 mg/L (IQR 0.8–4.2 mg/L). Levels were numerically higher in women compared with men (2.2 mg/L vs 1.5 mg/L). HsCRP categorised 75 (38%) patients as having a high level (>3 mg/L) with 65 (33%) and 58 (29.3) at intermediate (1–3 mg/L) and low (<1 mg/L) levels. Levels of hscTnI and hsCRP did not differ when stratified by site (online supplemental table S2).

Using the sex stratified Framingham laboratory-based risk score with lipids, the majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Although sample sizes remained limited when stratified by sex and risk category, the prevalence of hypertension remained higher in women compared with men (table 3) and as expected higher in the intermediate and high-risk groups across the population (online supplemental table S3).

Association between hscTnI and hsCRP and traditional cardiovascular risk factors were also evaluated (table 4). The findings from cumulative logit models showed that older patients were more likely to have higher hscTnI levels (adjusted OR (aOR) per year: 1.05, 95% CI 1.01 to 1.09, p<0.011). Female patients, compared with male patients, were identified as having lower hscTnI levels. SBP of 140–159 mm Hg and SBP >160 mm Hg were associated with higher hscTnI concentrations (aOR 2.96 (95% CI 1.09 to 7.90, p=0.030) and 4.68 (95% CI 1.55 to 14.1, p=0.006), respectively) compared with those with SBP <130 mm Hg. Our study did not find any strong associations between hsTnI and traditional cardiovascular risk factors including age, hypertension, diabetes and smoking. We also did not find any association between SBP levels and hscTnI. Levels of hscTnI were higher for HIV-patients with higher hscTnI levels. Study site—as a surrogate for socioeconomic status—was not associated with hscTnI or hsCRP.

### DISCUSSION

In this small, descriptive, cross-sectional study across two sites in urban Kenya, we evaluated the prevalence of traditional cardiovascular risk factors. We also explored how biochemical markers of inflammation and myocardial injury are associated with traditional cardiovascular risk factors in PLHIV. We make a number of observations. First, in a relatively young population with HIV, some traditional cardiovascular risk factors were common. Smoking and diabetes rates, however, were low. Second, using traditional risk estimation systems, the majority of the young HIV population were categorised as low-risk for future cardiovascular events. Third, across the majority of patients, hstnI values were below the limit of detection. Fourth, in exploratory analysis we found no associations between hsCRP levels and traditional cardiovascular risk factors but did observe a positive association between hscTnI levels and increasing age and higher SBP.

Some traditional cardiovascular risk factors were common in the HIV population studied. Hypertension was self-reported in one in five individuals and higher, at one in three, when classified by office SBP measurement and/or use of anti-hypertensives. Self-reported...
Table 4  Relationship between baseline markers of myocardial injury and inflammation and traditional cardiovascular risk factors, displayed as multivariable-adjusted ORs* for high-sensitivity cardiac troponin I and multivariable-adjusted mean differences† for hsCRP

| Risk factor                  | Model I AOR (95% CI) | Model II AOR (95% CI) | Model III AOR (95% CI) | Model I AOR (95% CI) | Model II AOR (95% CI) | Model III AOR (95% CI) | Model I Adjusted Coef. (95% CI) | Model II Adjusted Coef. (95% CI) | Model III Adjusted Coef. (95% CI) |
|------------------------------|----------------------|-----------------------|------------------------|----------------------|-----------------------|------------------------|---------------------------------|---------------------------------|---------------------------------|
| Age (years)                  | 1.05 (1.02 to 1.09, p=0.004) | 1.05 (1.01 to 1.09, p=0.021) | 1.04 (1.00 to 1.08, p=0.032) | 0.004 (−0.12 to 0.12, p=0.952) | 0.01 (−0.11 to 0.14, p=0.860) | 0.02 (−0.13 to 0.17, p=0.775) |
| Sex                          |                       |                       |                        |                      |                       |                        |                                 |                                 |                                 |
| Male                         | Reference             | Reference             | Reference              | Reference            | Reference            | Reference              |                                 |                                 |                                 |
| Female                       | 0.32 (0.14 to 0.70, p=0.004) | 0.39 (0.16 to 0.93, p=0.035) | 0.38 (0.17 to 0.84, p=0.018) | 1.66 (−0.85 to 4.18, p=0.194) | 1.49 (−1.28 to 4.25, p=0.290) | 0.04 (−3.39 to 3.47, p=0.980) |
| Study site                   | AKUNH                 |                       |                        |                      |                       |                        |                                 |                                 |                                 |
| Coptic                       | 1.08 (0.54 to 2.16, p=0.832) | 0.97 (0.48 to 1.99, p=0.941) | 0.91 (0.44 to 1.90, p=0.805) | 0.78 (−1.70 to 3.27, p=0.536) | 0.91 (−1.63 to 3.45, p=0.481) | 0.87 (−2.02 to 3.76, p=0.553) |
| Hypertension                 | −                     | 2.76 (1.36 to 5.63, p=0.005) | −                       | −                     | −1.23 (−3.91 to 1.45, p=0.366) | −                       |                                 |                                 |                                 |
| Diabetes                     | −                     | 0.53 (0.06 to 3.37, p=0.513) | −                       | −                     | 0.41 (−6.24 to 7.06, p=0.903) | −                       |                                 |                                 |                                 |
| Smoking                      | Never smoker          | Reference             | Reference              | −                     | −                     | Reference              | −                                 |                                 |                                 |
| Former smoker                | −                     | 1.19 (0.51 to 2.70, p=0.685) | −                       | −                     | −0.45 (−3.61 to 2.72, p=0.781) | −                       |                                 |                                 |                                 |
| Current smoker               | −                     | 1.36 (0.15 to 9.11, p=0.762) | −                       | −                     | 0.22 (−7.47 to 7.92, p=0.954) | −                       |                                 |                                 |                                 |
| Systolic blood pressure      |                       |                       |                        |                      |                       |                        |                                 |                                 |                                 |
| SBP <130 mm Hg               | Reference             | −                     | Reference              | −                     | −                     | Reference              | −                                 |                                 |                                 |
| SBP 130–139 mm Hg            | −                     | −                     | 2.29 (0.87 to 5.87, p=0.087) | −                     | −                     | −2.40 (−6.37 to 1.58, p=0.235) |
| SBP 140–159 mm Hg            | −                     | −                     | 3.08 (1.13 to 8.34, p=0.028) | −                     | −                     | −3.47 (−8.13 to 1.19, p=0.143) |
| SBP >160 mm Hg               | −                     | −                     | 5.40 (1.75 to 16.6, p=0.003) | −                     | −                     | −2.09 (−7.45 to 3.26, p=0.441) |
| High-sensitivity CRP ng/L    | −                     | −                     | 1.05 (1.01 to 1.10, p=0.014) | −                     | −                     | −                       |                                 |                                 |                                 |
| High-sensitivity troponin-I  |                       |                       |                        |                      |                       |                        |                                 |                                 |                                 |
| <2.50 ng/L                   | Reference             | Reference             | Reference              | Reference            | Reference            | Reference              | 4.42 (0.78 to 8.07, p=0.018) |                                 |                                 |
| 2.50–3.02 ng/L               | −                     | −                     | −                       | −                     | −                     | −                       |                                 |                                 |                                 |
| 3.02–7.12 ng/L               | −                     | −                     | −                       | −                     | −                     | −                       | 1.20 (−2.43 to 4.84, p=0.514) |                                 |                                 |
| ≥7.12 ng/L                   | −                     | −                     | −                       | −                     | −                     | −                       | 0.57 (−3.23 to 4.38, p=0.766) |                                 |                                 |

Continued
Table 4 Continued

| Risk factor       | Model I AOR (95% CI) | Model II AOR (95% CI) | Model III AOR (95% CI) | Model I Adjusted Coef. (95% CI) | Model II Adjusted Coef. (95% CI) | Model III Adjusted Coef. (95% CI) |
|-------------------|----------------------|-----------------------|------------------------|---------------------------------|---------------------------------|----------------------------------|
| Creatinine mg/L   | 1.00 (0.99 to 1.03, p=0.671) | 1.01 (0.99 to 1.03, p=0.399) | 1.01 (0.99 to 1.04, p=0.177) | −0.01 (−0.05 to 0.02, p=0.568) | −0.01 (−0.04 to 0.03, p=0.644) | −0.11 (−0.20 to −0.03, p=0.010) |

*Cumulative logit model with high-sensitivity troponin-I response as myocardial injury marker. Bold p values indicate statistical significance (p<0.05). Model I adjusts for age, sex, creatinine and study site; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as Model I plus systolic blood pressure and hsCRP levels.

†Linear regression with high-sensitivity C-reactive protein (hsCRP) response as inflammation marker. Bold p values indicate statistical significance (p<0.05). Model I adjusts for age, sex and creatinine; Model II as for Model I plus history of hypertension, diabetes and smoking status; Model III as Model I plus systolic blood pressure and hsCRP levels.

AKUHN, Aga Khan University Hospital, Nairobi; AOR, adjusted OR; Coef., coefficient as multivariable mean difference; Coptic, Coptic Hope Center for Infectious Diseases.

Dyslipidaemia was low at 1 in 20 but much higher when based on total cholesterol concentration >6.1 mmol/L (19%). This discordance likely reflects individuals being unaware of their cholesterol status. Smoking and diabetes rates, however, remained relatively low in contrast to PLHIV in high-income countries. Our prevalence rates of traditional cardiovascular risk factors are in agreement with other studies from the sub-Saharan African region and discordant to those evaluating PLHIV in high-income settings. While North American/European studies contribute to most of the evidence evaluating CVD in HIV, the region only hosts 6% of the global HIV population compared with 75% for sub-Saharan Africa. PLHIV in sub-Saharan Africa and North America/Europe are different by virtue of the factors associated with HIV acquisition. HIV remains firmly established in the general population in sub-Saharan Africa but overwhelmingly affects men who have sex with men and intravenous drug users in North America/Europe. These differences probably account for regional discordance in the association between HIV status and prevalence of cardiovascular risk factors that has been observed in the published literature. Positive associations in North America/Europe either become null or even reverse in sub-Saharan Africa.

Using the sex stratified Framingham laboratory-based risk score, the overwhelming majority of the HIV population was classified at low risk (83%) with 12% at intermediate risk and 5% at high risk. Similar risk categorisations were obtained when using the Framingham non-laboratory-based risk scores. All established cardiovascular risk estimation systems—predominantly developed in high-income countries and not accounting for HIV status—are highly influenced by age. As such, our findings likely reflect the younger age distribution in our study. Whether this estimation of low-risk, using generalised risk scores developed predominantly in high-income countries, reflects the observed cardiovascular risk of HIV individuals in sub-Saharan Africa remains uncertain.

Previous studies have shown how biochemical markers, such as hsCRP and hscTnI, may hold promise in improving cardiac risk estimation systems. Our study showed that the majority of individuals had undetectable levels of hscTnI with only one in three patients demonstrating levels above the limit of detection. Previous studies in high-income settings have shown that during acute HIV infection, troponin levels are higher but drop threefold once viremic control is achieved. A large proportion of our patients were established on ART and with the duration of diagnosis to study recruitment being nearly 12 years. Two studies showed contrasting results when evaluating the association between troponin levels and presence of coronary plaques, with results primarily applicable to men with HIV in non-endemic regions. Levels of hsCRP, suggestive of underlying inflammation, were high in this study with women having higher concentrations. Whether higher baseline hsCRP levels relate to increased risk of cardiovascular events in HIV, however, remains uncertain with contrasting data in the published literature.

Higher levels of hsCRP in people with HIV is biologically plausible and supported by previous studies, but may not just be reflective of vascular disease. As such the specificity of hsCRP for CVD in PLHIV may be low.

Our study showed, hscTnI levels were higher in men, associated with increasing age, measured SBP and reported history of hypertension. This is similar to what has been observed in the general population. However, surprisingly, in our study, much of the population had troponin concentrations below the limit of quantification despite using a high-sensitivity assay likely reflective of a younger population. Unlike in the general population, we did not show any robust association between hsCRP and traditional cardiovascular risk factors. This may reflect the younger age of our population with previous studies showing higher hsCRP values in the elderly.

This is one of the few studies that has quantified the prevalence of cardiovascular risk factors and explored their association with biochemical markers of inflammation and myocardial injury in HIV populations from two distinct centres in urban Kenya. However, several limitations should be considered. First, our study was cross-sectional and we were unable to evaluate the associations...
between novel biochemical markers and future cardiovascular events. Second, HIV populations in our study were recruited across two centers in Nairobi, representing a predominantly urban population. Whether our findings are generalisable to rural populations remains uncertain. Third, given resource limitations, we did not study age-matched and sex-matched non-HIV populations and were limited to a finite choice of biochemical biomarkers.

As such our study is unable to comment on associations between a wider range of biochemical markers and cardiovascular risk factors in the general population and how these may differ to those infected with HIV. For the same reason we were also unable to measure metric if infection control (viral load and CD4 count) at the time of recruitment. Fourth, some of the risk factors such as diabetes status depended on self-reporting—as such, the absence of associations may reflect exposure misclassification. Lastly, we cannot exclude the possibility that associations between biomarkers and outcomes may in part be due to residual confounding or unmeasured confounders.

CONCLUSIONS

In conclusion, we show that while some traditional cardiovascular risk factor prevalences remain high in HIV populations in sub-Saharan Africa, important ones such as smoking are low. This is in contrast to HIV populations in non-endemic regions. The majority of PLHIV—using traditional risk estimation systems—have a low estimated CVD risk likely reflecting a younger aged population predominantly consisting of women. While hsTnI values were associated with increasing age and higher blood pressure, no associations between hsCRP levels and traditional cardiovascular risk factors were observed.

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Contributors

ASVS and MHC conceived and designed the study. HAA recruited the patients. ASVS and HAA wrote the first draft of the manuscript. IGA, HAA and JS analysed the data. ASVS, JM, IGA, KKL, SRA, PP, JS, MKA, SE and MHC made critical revisions on the paper. ASVS is the author acting as guarantor for the study.

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Competing interests

ASVS’s institution has received speaker fees from Abbott Diagnostics. The authors declare no other conflicts of interest.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication

Not applicable.

Ethics approval

This study involves human participants and was approved by The Aga Khan University Hospital Research Ethics Committee. Ref: 2018-REC-24. Participants gave informed consent to participate in the study before taking part.

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Data availability statement

Data are available upon reasonable request. Data will be available on request to the corresponding author (nhanoo.shah@tsihtm.ac.uk).

Supplemental material

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