



HIV with non-communicable diseases in primary care in Kibera, Nairobi, Kenya: characteristics and outcomes 2010–2013

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Background: Antiretroviral therapy (ART) has increased the life expectancy of people living with HIV (PLHIV); HIV is now considered a chronic disease. Non-communicable diseases (NCDs) and HIV care were integrated into primary care clinics operated within the informal settlement of Kibera, Nairobi, Kenya. We describe early cohort outcomes among PLHIV and HIV-negative patients, both of whom had NCDs.

Methods: A retrospective analysis was performed of routinely collected clinic data from January 2010 to June 2013. All patients >14 years with hypertension and/or diabetes were included.

Results: Of 2206 patients included in the analysis, 210 (9.5%) were PLHIV. Median age at enrollment in the NCD program was 43 years for PLHIV and 49 years for HIV-negative patients ($p < 0.0001$). The median duration of follow up was 1.4 (IQR 0.7–2.1) and 1.0 (IQR 0.4–1.8) years for PLHIV and HIV-negative patients, respectively ($p = 0.003$). Among patients with hypertension, blood pressure outcomes were similar, and for those with diabetes, outcomes for HbA1c, fasting glucose and cholesterol were not significantly different between the two groups. The frequency of chronic kidney disease (CKD) was 12% overall. Median age for PLHIV and CKD was 50 vs 55 years for those without HIV ($p = 0.005$).

Conclusions: In this early comparison of PLHIV and HIV-negative patients with NCDs, there were significant differences in age at diagnosis but both groups responded similarly to treatment. This study suggests that integrating NCD care for PLHIV along with HIV-negative patients is feasible and achieves similar results.

Keywords: Africa, Chronic kidney disease, Diabetes, HIV, Hypertension, Non-communicable diseases

Introduction

With the successful scale-up of antiretroviral therapy (ART) programmes, life expectancy of people living with HIV (PLHIV) has increased, and HIV is now considered a chronic disease.¹ There is evidence that HIV infection and ART are both risk factors for the development of non-communicable diseases (NCDs) in resource-limited settings.^{2–5} Within Africa, there is an ongoing demographic and epidemiologic transition of disease burden from infectious diseases to NCDs due to rapid urbanization, improved healthcare and economic changes.⁶ As a result, populations are increasingly demonstrating comorbid NCDs, such as hypertension, diabetes and kidney disease, with HIV.⁷

Health care providers are now faced with an increasing need to manage HIV and NCDs simultaneously. Provision of comprehensive integrated primary care incorporating chronic disease management

along with HIV care and treatment in Africa would appear to be a natural progression of current primary care programs. However, little is known regarding the identification and management of chronic diseases in Africa, especially when associated with HIV.^{7–9} It is frequently difficult for patients to afford services for NCDs and often there are significant geographic constraints to accessing services.¹⁰ In addition, in many informal settlements, such as Kibera, Nairobi, Kenya, the population is often mobile. Delivering consistent long-term chronic disease services and minimizing the loss to follow-up (LTFU) of patients are top priorities in maintaining quality care. We are not aware of any previous studies directly comparing NCD outcomes of PLHIV versus those who are HIV-negative in sub-Saharan Africa.

Since 2010, Médecins Sans Frontières (MSF) has operated a primary care programme in the informal settlement of Kibera, caring for patients with chronic diseases, including hypertension,

diabetes mellitus and chronic kidney disease (CKD). The experiences derived from the provision of ART in such populations, including treatment literacy, access to free medications and care, were applied with the integration of NCD and HIV/TB care in primary care clinics in Kibera. The program is notable in that it has used clinical officers and nurses as the main caregivers and employs standardized treatment protocols.

We describe a cohort of patients with NCDs comparing presenting characteristics and preliminary outcomes between those who were HIV positive and negative.

Methods

Study design and setting

This is a retrospective descriptive cohort study of routinely collected program data.

The study was conducted in Kibera, which is an informal settlement located in Nairobi, Kenya, and is one of the largest of this kind in Africa with an estimated total population of 235 000–270 000.¹¹ Kibera is characterized by high poverty levels, lack of formal infrastructure and sanitation, an estimated HIV prevalence of 12.6% (about twice the national prevalence of 6.2%) and minimal governmental health care.¹² MSF operates two primary care clinics within Kibera that provide integrated care for HIV, TB, acute illnesses, maternal–child care, malnutrition and, since 2010, chronic diseases. MSF clinics are the only provider of comprehensive primary care services in Kibera; a key component is that treatment and medication are offered free of charge.

HIV care has been provided in Kibera since 2003 and currently follows the national ART guidelines. At the time of the study, first line ART utilized tenofovir/lamivudine/efavirenz and second line treatment used lopinavir/ritonavir instead of efavirenz. Standard protocols for frequency of visits and laboratory monitoring, initially with CD4 and more recently with viral load, were defined within the program. Screening blood pressure monitoring was done at each visit on all adults with HIV; however, glucose screening was only completed if the patient was symptomatic, had a history of diabetes or elevated glucose levels with other testing.

Prior to establishing the NCD chronic disease health care package in Kibera, available national and international guidelines were reviewed. Medications were chosen for specific illnesses and guidelines were written as to how and when each medication was to be prescribed, as well as when follow-up was required, including routine laboratory monitoring. These protocols were aligned as far as possible with current NCD guidelines and have been previously described.¹³ All adults and adolescents presenting to the clinics had their blood pressure recorded at each visit to screen for hypertension. Screening for diabetes was only done if the patient had a history of diabetes, elevated glucose (on lab work during evaluation or follow up of HIV, hypertension or an acute illness) or was symptomatic with polyuria, polydipsia and/or polyphagia.

For hypertension management, the protocol suggested medication choices including enalapril, hydrochlorothiazide, nifedipine sustained release and atenolol. The target blood pressure goal was <140/90 unless patients had chronic kidney disease with proteinuria or diabetes for whom the goal was <130/80. For diabetes care, only the use of metformin and glibenclamide were available. Insulin treatment was beyond the scope of practice for clinical

officers within the MSF clinics and patients requiring insulin were referred to the Ministry of Health diabetes clinic for care. The target for glucose control was a fasting plasma glucose of <6.8 mmol/L or an HbA1c <7.0%. For those with hyperlipidemia the goal was a total cholesterol <5.2 mmol/L.

The multidisciplinary clinical team (clinical officers, nurses, mental health counselors, nutritionists and social workers) were trained on the diagnosis and management of chronic diseases utilizing the new protocols, which included both life style changes and medication interventions. Consideration was given to possible medication side effects and interactions, particularly when prescribed concurrently with ART.

Study population

All patients who were 15 years of age or older, with or without HIV infection, registered in the chronic diseases clinic with hypertension and/or diabetes mellitus from January 2010 through June 2013 were included in the study.

Data collection and variables

Data were collected systematically during routine clinic visits into a chronic disease collection tool. At intake they included patient demographics, clinical characteristics of body mass index (BMI), systolic and diastolic blood pressure, serum creatinine, total cholesterol, fasting glucose. In addition, for PLHIV at intake, clinical characteristics (HIV staging, CD4 count, years on ART and years in the MSF ART program) were collected. Creatinine clearance was calculated using a previously validated formula in Kenya: the Chronic Kidney Disease Epidemiology Consortium (CKD-EPI) equation.¹⁴ CKD was defined as a creatinine clearance <60 ml/min and staged using international guidelines.¹⁵

For patients with hypertension in follow-up for 6 months or longer, outcome variables included systolic and diastolic blood. For patients with diabetes followed longer than 6 months, outcome variables included fasting glucose and total cholesterol. HbA1c measurements were introduced in 2012 and were used to follow-up glucose control after enrollment. PLHIV and HIV-negative patients who had NCDs were seen every 3–6 months for routine follow-up or more frequently if indicated. LTFU was defined as patients not seen in the previous 6 months or longer. Defaulter tracing was routinely used for PLHIV, but not with patients with NCDs alone.

Data were entered into a dedicated database (EpiData v3.1, EpiData Association, Odense, Denmark) each day following clinic visits.¹⁶ Data on PLHIV were also recorded in the Follow-up and Care of HIV Infection and AIDS (FUCHIA) database software (Epicentre, Paris, France).¹⁷ A standardized data collection tool (EpiData) was utilized to capture patient-specific data from both databases for analysis and comparison. Data identifiers for PLHIV in both databases were matched for correlation. Patients with missing data had file reviews completed and were logged and updated into the new combined database if data were available.

Analysis

Statistical analysis was performed using the Epi Info 7 Analysis software.¹⁸ Descriptive statistics were completed by calculating the median and IQR for continuous data and proportions for

categorical data. Assessment of selected outcomes of PLHIV versus HIV-negative patients were conducted. Comparisons between group proportions were performed using Fisher's exact test with a 5% level of significance. As most continuous data were not normally distributed, comparisons were made with the Wilcoxon rank sum test, with a 5% level of significance. Age-adjustment using the HIV-negative population as reference population was conducted when indicated.

Ethics review

For this study, routinely collected MSF data was retrospectively reviewed and de-identified. Hence, informed consent from patients or their families was not obtained by treating clinicians.

The Ethics Review Board at the Kenya Medical Research Institute in Nairobi approved this study. It met the MSF (Geneva, Switzerland) Ethics Review Board-approved criteria for analysis of routinely collected program data. It also satisfied the requirements of the Ethics Advisory Group of the International Union against Tuberculosis and Lung Disease, Paris, France, and met their approval.

Results

Between January 2010 and June 2013, 2206 patients were enrolled in the NCD program. Demographics and clinical

characteristics are shown in Table 1. Of those enrolled, 9.2% (144/1567) of females and 10.3% (66/639) of males were PLHIV. Among those who were HIV-negative, 71.3% (1423/1996) were female and 28.7% (573/1996) were male. Individuals with HIV were significantly younger than those without. BMI was significantly lower when comparing both male and female PLHIV vs HIV-negative: males 21 vs 23 ($p=0.02$) and females 25 vs 28 kg/m² ($p<0.001$), respectively. In comparing the proportion of patients by presenting hypertension stage, PLHIV presented more frequently with stage 1 and those without HIV had significantly more cases in stage 3.

A total of 309 patients were diagnosed with diabetes, of whom 39 had type 1 diabetes, and none of which were PLHIV. A higher proportion of patients without HIV had diabetes than PLHIV, 15.0% (299/1996) versus 4.8% (10/210), respectively ($p<0.0001$). There were no significant differences in measured BMI between the groups.

The clinical characteristics of PLHIV at enrollment in the NCD cohort are described in Table 2. The median period (4 years) on antiretroviral medications was similar for men and women, while the median CD4 count was higher for men.

The frequency of CKD (CKD = creatinine clearance <60 ml/min) in the combined cohort was 12.1% (217/1801). An age-adjusted analysis of CKD frequency among PLHIV showed a slightly higher result of 17%. Of those with CKD within the cohort, 13.4% (29/217) had concurrent Type 1 or 2 diabetes mellitus.

Table 1. Enrollment characteristics of people living with HIV and HIV negative in the chronic disease cohort, Kibera, Nairobi, Kenya 2010–2013

Demographic and clinical characteristics	HIV negative	PLHIV	p-value
Number of patients (%)	1996 (90.5)	210 (9.5)	NA
Median age years at enrollment into chronic disease program (IQR)	49 (40–56)	43 (39–50)	$p<0.0001$
Frequency of hypertension (%) (n=1697 HIV negative, 200 PLHIV)			
Stage 1 hypertension (SBP 140–159 or DBP 90–99)	525 (30.9)	88 (44.0)	$p<0.0003$
Stage 2 hypertension (SBP 160–179 or DBP 100–109)	564 (33.2)	78 (39.0)	NS
Stage 3 hypertension (SBP \geq 180 or DBP \geq 110)	558 (32.9)	29 (14.5)	$p<0.0001$
Isolated systolic hypertension (SBP \geq 140 and DBP $<$ 90)	50 (2.9)	5 (2.5)	NS
Frequency of diabetes (%) ^a (n=299 HIV negative, 10 PLHIV)			
Type 1	39 (13.0)	0 (0.0)	NA
Type 2	260 (86.9)	10 (100.0)	NS
Chronic kidney disease ^b (%) (n=1612 HIV negative, 188 PLHIV)			
Stage 1 (\geq 90 ml/min)	478 (29.7)	68 (36.2)	NS
Stage 2 (60–89 ml/min)	951 (58.9)	95 (50.5)	NS
Stage 3 (30–59 ml/min)	168 (10.4)	20 (10.6)	NS
Stage 4 or 5 ($<$ 30 ml/min)	15 (1.0)	5 (2.7)	NS

NA: not applicable; NS: not significant; PLHIV: people living with HIV.

^a Diagnosis of diabetes was fasting plasma glucose \geq 7.0 mmol/L (126 mg/dl) or 2 hour post-75 g glucose load \geq 11.1 mmol/L (200 mg/dl).

^b Chronic kidney disease stage was determined using an estimated glomerular filtration rate by the CKD-EPI formula and was co-morbid with either hypertension or diabetes.

Table 2. Clinical characteristics of people living with HIV in the chronic disease cohort at enrollment in Kibera, Nairobi, Kenya 2010–2013

Clinical characteristics	Male (n=66)	Female (n=144)	p-value
Median age, years, at FUCHIA enrollment (IQR)	43 (36–50)	40 (34–46)	NS
Median CD4 count at enrollment in chronic disease program (IQR)	476 (339–578)	442 (305–554)	NS
Median years in HIV program (IQR)	4 (3–6)	5 (3–7)	NS
Median years on ART (IQR)	4 (3–6)	4 (2–6)	NS

ART: antiretroviral treatment; FUCHIA: Follow-Up and Care of HIV Infection and Aids programme; NS: not significant.

Table 3. Selected outcomes of people living with HIV and HIV negative in the chronic disease cohort at enrollment in Kibera, Nairobi, Kenya 2010–2013

Outcome variables	HIV negative (n=1996)	PLHIV (n=210)	p-value
Median duration of follow-up, years (IQR)	1.0 (0.4–1.8)	1.4 (0.7–2.1)	p=0.003
Frequency of lost to follow-up >6 months (%)	721 (36.1)	46 (21.9)	p<0.0001
Median systolic blood pressure in patients with hypertension, mm Hg (n=1696 HIV negative, 200 PLHIV)			
At enrollment (IQR)	160 (144–177)	151 (136–164)	p<0.0001
Last visit	141 (129–158)	143 (129–159)	NS
Median diastolic blood pressure in patients with hypertension, mm Hg (n=1697 HIV negative, 200 PLHIV)			
At enrollment (IQR)	100 (90–110)	97 (86–105)	p=0.001
Last visit	87 (75–95)	85 (74–95)	NS
Median fasting total cholesterol in patients with diabetes, mmol/L (n=209 HIV negative, 10 PLHIV)			
At enrollment (IQR)	5.3 (4–6)	6.3 (5–7)	NS
Last visit	5.0 (4–6)	5.6 (5–6)	NS
Median fasting blood glucose in patients with diabetes, mmol/L (n=209 HIV negative, 10 PLHIV)			
At enrollment (IQR)	10.7 (7–14)	12.5 (9–16)	NS
Last visit	8.0 (6–11)	8.6 (8–12)	NS
Median HbA1c in patients with diabetes ^a (n=209 HIV negative, 10 PLHIV)			
Last visit	8.8 (7–11)	8.2 (7–11)	NS

NS: not significant; PLHIV: people living with HIV.

^a HbA1c was not a routine measurement at enrollment to the chronic disease program and only ordered every 6 months after treatment began.

There was no association found between the use of tenofovir and CKD among PLHIV. The median age for those with PLHIV and CKD was 50 (IQR 36–54) vs 55 (47–65) years for those without HIV (p=0.005).

Median duration of follow-up was 1.4 (IQR 0.7–2.1) and 1.0 (IQR 0.4–1.8) years for PLHIV and HIV-negative patients, respectively (p=0.003) see Table 3. Over the study period, systolic blood pressure (SBP) and diastolic blood pressure (DBP) outcomes were similar for PLHIV and those without HIV. For patients with hypertension who were followed at least 6 months or longer, the

proportion achieving their target SBP on the last visit was 40% (36/89) for PLHIV and was 50.0% (466/933) for HIV-negative patients; the proportion achieving their target DBP was 58% (52/89) for PLHIV and was 64.6% (603/933) for HIV-negative patients.

Among patients with diabetes, follow-up HbA1c, fasting glucose and cholesterol results were also similar without significant differences. The proportion of patients with diabetes with follow-up HbA1c results who reached a target HbA1c <7.0% was 37.5% (3/8) for PLHIV and 19.6% (26/133) for HIV-negative patients; the

proportion whose follow-up fasting glucose results reached a target of <6.8 mmol/L was 12.5% (1/8) for PLHIV and 38.0% (82/216) for HIV-negative patients; and the proportion whose follow-up fasting total cholesterol results reached a target of <5.2 mmol/L was 37.5% (3/8) for PLHIV and 60.8% (90/148) for HIV-negative patients. Rates of LTFU were higher for people without HIV. Eight patients died during the study (five males and two females who were HIV-negative, one PLHIV female).

Discussion

To our knowledge this study provides the first direct comparison of early NCD outcomes for PLHIV and those without HIV from sub-Saharan Africa. It offers a unique look at a population from an informal urban settlement context, which is considered to be the epicenter of the epidemiological transition for NCDs in sub-Saharan Africa.¹⁹ The findings in this study suggest that PLHIV would likely benefit from NCD screening and treatment within similar HIV programs.

There was a notably larger proportion of women in the overall cohort, which has been reported previously.¹³ This is believed to be mainly secondary to the focus of the MSF health package on women and children in Kibera, but there may be other factors involved. The median age of enrollment for hypertension and/or diabetes was found to be significantly younger in PLHIV. This may be partly related to the ongoing routine follow-up of PLHIV and their earlier presentation for HIV care. However, HIV has been associated with an increased risk of developing cardiovascular disease by others.^{2,9,20} This is of particular importance because if PLHIV are developing NCDs earlier than their counterparts, it could be argued that they are a group in which earlier screening might be valuable.⁹ With earlier detection of diseases such as hypertension, diabetes and CKD, interventions would have a higher likelihood of preventing complications. This study suggests that screening and treating patients for NCDs within established HIV programmes, such as in Kibera, is feasible and could produce outcomes comparable to patients without HIV.

On presentation, PLHIV had both lower BMIs and stages of hypertension overall in comparison to HIV-negative patients. These findings are consistent with an earlier age of diagnosis in PLHIV. Of those who were treated for hypertension, there were similarly good improvements in blood pressure, regardless of HIV status. Comparable outcomes were also seen for patients with diabetes for follow-up fasting glucose, cholesterol and HbA1c measurements. This would suggest that current treatment protocols and medications are effective for both PLHIV and those without HIV within this primary care program. It also demonstrates that using a standardized treatment approach, employing clinical officers and nurses (instead of physicians) in a highly resource-constrained setting, NCDs can be managed in an integrated fashion, concurrently with HIV.

The earlier detection of an NCD was most notable among those with HIV and CKD using the CKD-EPI formula, which was recently validated in Kenya among ART-naïve patients with HIV.¹⁴ Among patients with concurrent CKD, PLHIV had a median 5 year earlier onset of CKD compared to those who were HIV negative. A sub-analysis did not find any association with the use of tenofovir, as has been previously documented.²¹ It is believed that PLHIV, particularly those of African descent, have a higher prevalence of renal dysfunction secondary to HIV infection.^{22,23}

Also notable was that the frequency of CKD was not as strongly related to diabetes (13%) as in developed countries, where it is a comorbidity in more than 40% of cases.²⁴ This result implies that those who live within this context are more likely to develop CKD from other causes such as hypertension, glomerulonephritis or TB nephritis. Similar conclusions have been reported by others.²⁵ This finding should increase the awareness of a need to focus on earlier recognition of these other potential causes of CKD, and further study is essential to better define the epidemiology of CKD in sub-Saharan Africa, as has been suggested by other authors.²⁶

There is extremely limited dialysis availability in developing countries and none in many regions of sub-Saharan Africa.²⁷ Therefore, it appears critical that PLHIV with NCDs be monitored for CKD, particularly as they mature, so that early treatment with an antihypertensive medication, when indicated, can be instituted to help slow the progression to what will otherwise certainly be a fatal disease in this context.^{23,26}

The median duration of follow-up was shorter among those who were HIV-negative versus PLHIV, 1 and 1.4 years respectively. This is felt to be largely due to the high LTFU rate after six months, which was 36% in HIV-negative patients versus 22% in PLHIV. Similar findings have been reported in two other studies of the MSF Kibera programme.^{13,28} The high LTFU may be related to the transient nature of the inhabitants of Kibera: many have primary homes in rural Kenya and move between both residences during holidays and other times. Regardless, the lower LTFU among those PLHIV could suggest that routine defaulter tracing and counseling, only employed for this group, may lead to lower LTFU in the non-HIV group. This is an area that needs further exploration and study.

With the advancement of wide spread antiretroviral medication use in sub-Saharan Africa and subsequent viral load suppression, the life span of those PLHIV will approach that of those uninfected. Thus, HIV itself is becoming a chronic disease and PLHIV will have a higher risk of dying secondarily due to an NCD rather than the HIV infection itself. The problem of the increasing NCD burden is compounded in countries like Kenya where care for NCDs is not widely accessible or free of charge. Components of this problem are a lack of health care providers trained in NCD management, relevant national guidelines and access to medications free of cost. This challenge was recently reported by a study done in a comparable Nairobi slum, where of those found to have hypertension on screening, only 19.5% knew they had high blood pressure and $<3\%$ were being adequately treated.²⁹ Similar findings have been reported regarding diabetes awareness in another recent study in Kibera.³⁰

To adequately meet the healthcare needs of this population, increased access to quality NCD care, free medication and the development of national guidelines should be supported both within Kenya and other similar settings. Primary health care should be a right for all, not a privilege of few. Addressing NCDs today presents a remarkably similar set of challenges to that of HIV only 10 years ago in 2005.

The strengths of this study were that it reflects the 'real world results' of a primary care program from within an urban informal settlement, it used clear treatment protocols and maintained routine data collection, particularly regarding LTFU. The main weakness was that this was an operational study with retrospective review of observational data and its associated challenges.³¹ In

addition, there was a preponderance of females overall and a relatively small comparative cohort of PLHIV with NCDs, especially among the diabetic group. Further studies need to be conducted on a larger group of patients with NCDs, looking specifically at outcomes such as HbA1c and changes in creatinine clearance over time. Lastly, it remains unclear as to what age and BMI screening for NCDs should begin in PLHIV, especially for diabetes mellitus in this context, and needs more research.

Conclusions

This study highlights the need to recognize the increasing chronic disease burden in sub-Saharan Africa. PLHIV are at higher risk of developing concurrent NCDs at a younger age and would benefit from routine screening and treatment. Treatment appears to produce results comparable to patients without HIV. It also demonstrates that it is possible to integrate both HIV and NCD care together in a primary care program that is largely run by clinical officers and nursing staff within significant resource constraints. This model may be useful in the scale-up of NCD care in sub-Saharan Africa in the future.

Authors' contributions: JKE, HB and AS conceived the study; JKE, AS, RVB, WK, AS, RJK and TR designed the study protocol; JKE, WK, EC, RVB carried out the analysis of these data. JKE drafted the manuscript; HB, RVB, RJK, AS, SNV, AV, EC, WK and TR critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. JKE is the guarantor of the paper.

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Competing interests: None declared.

Ethical approval: The Ethics Review Board at the Kenya Medical Research Institute in Nairobi approved this study. It met the Médecins Sans Frontières' (Geneva, Switzerland) Ethics Review Board-approved criteria for analysis of routinely collected program data. It also satisfied the requirements of the Ethics Advisory Group of the International Union against Tuberculosis and Lung Disease (Paris, France) and met their approval. The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

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