J Antimicrob Chemother 2019; **74**: 2024–2029
doi:10.1093/jac/dkz134 Advance Access publication 15 April 2019

Journal of Antimicrobial Chemotherapy

Prevalence of drug resistance mutations among ART-naive and -experienced HIV-infected patients in Sierra Leone

George A. Yendewa [1–3]*, Foday Sahr[4], Sulaiman Lakoh[4], Marta Ruiz[5], Lucia Patiño[5], Andrés Tabernilla[5], Gibrilla F. Deen[4], Momodu Sesay[6], Robert A. Salata[1,2] and Eva Poveda [5]

[1]Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, USA; [2]Division of Infectious Diseases and HIV Medicine, University Hospitals Cleveland Medical Center, Cleveland, OH, USA; [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; [4]College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leone; [5]Group of Virology and Pathogenesis, Galicia Sur Health Research Institute (IIS Galicia Sur)-Complexo Hospitalario Universitario de Vigo, SERGAS-UVigo, Vigo, Spain; [6]National HIV/AIDS Secretariat, Freetown, Sierra Leone

*Corresponding author. Division of Infectious Diseases and HIV Medicine, University Hospitals Cleveland Medical Center, 11100 Euclid Ave., Cleveland, OH 44106, USA. E-mail: gay7@case.edu orcid.org/0000-0002-8474-1812

Received 1 January 2019; returned 24 January 2019; revised 27 February 2019; accepted 6 March 2019

Objectives: The aim of this study was to assess the prevalence of HIV drug resistance (HIVDR) in HIV-infected ART-naive and -experienced patients in Sierra Leone.

Patients and methods: We conducted a cross-sectional study of HIV-positive adults aged ≥18 years at Connaught Hospital in Freetown, Sierra Leone in November 2017. Sequencing was performed in the reverse transcriptase, protease and integrase regions, and interpreted using the Stanford HIVDR database and WHO 2009 mutation list.

Results: Two hundred and fifteen HIV-infected patients were included (64 ART naive and 151 ART experienced). The majority (66%) were female, the median age was 36 years and the median ART exposure was 48 months. The majority (83%) were infected with HIV-1 subtype CRF02_AG. In the ART-naive group, the pretreatment drug resistance (PDR) prevalence was 36.7% (14.2% to NRTIs and 22.4% to NNRTIs). The most prevalent PDR mutations were K103N (14.3%), M184V (8.2%) and Y181C (4.1%). In the ART-experienced group, 64.4% harboured resistance-associated mutations (RAMs) and the overall prevalence of RAMs to NRTIs and NNRTIs was 85.2% (52/61) and 96.7% (59/61), respectively. The most prevalent RAMs were K103N (40.7%), M184V (28.8%), D67N (15.3%) and T215I/F/Y (15.3%). Based on the genotypic susceptibility score estimates, 22.4% of ART-naive patients and 56% of ART-experienced patients were not susceptible to first-line ART used in Sierra Leone.

Conclusions: A high prevalence of circulating NRTI- and NNRTI-resistant variants was observed in ART-naive and -experienced HIV-1-infected patients in Sierra Leone. This necessitates the implementation of HIVDR surveillance programmes to inform national ART guidelines for the treatment and monitoring of HIV-infected patients in Sierra Leone.

Introduction

Sierra Leone is a low-income country in West Africa with >60% of its inhabitants living below the poverty line.[1] UNAIDS estimated a countrywide HIV prevalence rate of 1.7% in 2016 among people aged 15–49 years,[2] characterizing Sierra Leone as a low-prevalence country. Access to ART was severely limited in the country during previous decades but was scaled up after the civil war period (1989–2000). Notwithstanding these efforts, fewer than one-third (29%) of the country's estimated 60 000 HIV-infected people were on ART in 2015.[3] In response, the National HIV/AIDS Secretariat of Sierra Leone launched its National Strategic Plan (NSP) on HIV/AIDS in 2016 to combat the HIV epidemic. One of the key elements of the NSP was to provide ART to all HIV-positive individuals with a CD4 count <500 cells/mm^3, with the goal of expanding coverage to all HIV-positive individuals in the country by 2018 regardless of CD4 cell count.[3] The current ART guidelines for Sierra Leone (adapted from the WHO in 2006 and recently revised in 2017) recommend as first-line therapy a regimen based on a dual NRTI backbone plus either an NNRTI or a PI.[4]

The goals of ART are to achieve and maintain durable virological suppression in order to preserve or improve immunological function, prevent HIV transmission ('undetectable equals

untransmittable') and limit the emergence of drug resistance mutations (DRMs) that could lead to treatment failure.[5,6] The WHO 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection recommended viral load (VL) monitoring as the preferred approach to confirming treatment failure.[7] Routine VL monitoring is recommended at 6 and 12 months after ART initiation and every 12 months thereafter.[7] However, this technology is often unavailable or highly cost prohibitive in sub-Saharan Africa (SSA) where the majority of people living with HIV (PLWH) reside. Before the recent implementation of VL monitoring in Sierra Leone in 2016, CD4 cell count and WHO clinical staging were the mainstay by which treatment failure was accessed in the country.

The lack of capability to conduct pretreatment drug resistance (PDR) testing or to monitor patients already on ART (acquired drug resistance) in SSA has led to increasing prevalence of HIV drug resistance (HIVDR) in recent years. The WHO 2017 report on HIVDR revealed that the prevalence of PDR to NNRTIs during 2014–16 was >10% in three (Uganda, Namibia and Zimbabwe) of the four countries in SSA reporting data to the WHO.[8] Cameroon (the fourth country) reported a PDR prevalence of 8.1% to NNRTIs during the same period.[8] Several other studies from the West and Central Africa WHO region have reported high DRM rates, e.g.: 63% to NRTIs and 71% to NNRTIs in patients failing ART in Liberia;[9] 70%, 93% and 68% in Senegal, Mali and Guinea-Conakry, respectively;[10] 21.7% to NRTIs and 44.8% to NNRTIs in infants in Nigeria;[11] and up to 60% in a Guinea-Bissau cohort.[12] Thus, there are high levels of DRMs to NNRTIs, which currently constitute the recommended first-line ART in these countries. The problem may be of a much larger magnitude in countries that additionally lack VL monitoring capability to detect virological failure. Thus, the WHO 2016 consolidated guidelines encourage countries to conduct national HIVDR surveys to generate data locally that should inform choice of appropriate regimens at ART initiation.[7]

There are currently no published data describing HIVDR in Sierra Leone. In this cross-sectional study, we assessed the prevalence of HIVDR in a cohort of HIV-infected ART-naive and -experienced patients in Sierra Leone.

Patients and methods

HIV-infected adults aged ≥18 years who attend the HIV Clinic at Connaught Hospital in Freetown, Sierra Leone were enrolled in the study during November 2017. The clinic is the largest HIV facility in the country, providing services to >4000 adult PLWH. The study was approved by the Sierra Leone Ethics and Scientific Research Committee and the IRB of Case Western Reserve University/University Hospitals Cleveland Medical Center. Written informed consent was obtained from every study participant before enrolment into the study.

After obtaining written informed consent, demographic and clinical data were obtained from study participants. HIV testing was undertaken using the fourth-generation rapid test SD Bioline HIV-1/2 3.0 (Standard Diagnostics Inc). The Alere Pima™ Analyzer (Abbott Laboratories, Germany) was used to determine CD4 cell count. For each patient, 1 mL of frozen plasma (obtained by centrifuging whole blood at 2000 **g** for 10 min) was stored at −20°C in Sierra Leone before shipping on dry ice to the Galicia Sur Research Health Institute in Spain for molecular analysis. HIV reverse transcriptase (RT), protease (PR) and integrase (IN) were amplified from plasma using an in-house Sanger sequencing protocol (ANRS protocol, version January 2015, available at www.hivfrenchresistance.org). FASTA sequences were assembled using the Variant Reporter version 1.0 software (Thermo Fisher Scientific, USA) and aligned with the reference sequence HXB2 (GenBank accession number K03455.1). HIV genetic subtypes and DRMs were identified and interpreted using the Stanford HIVDR database (available at http://hivdb.stanford.edu). The genotypic susceptibility score (GSS), which depicts the number of active HIV drugs in a given combination ART regimen, was estimated using the Stanford HIVDR database as follows: susceptible and potential low-level resistance were scored as 1, low-level and intermediate resistance were pooled as intermediate and scored as 0.5, and high-level resistance was scored as 0. The GSS was calculated by summing the individual resistance scores for each first-line drug in the combination ART regimen. Finally, the WHO 2009 mutation list was used to calculate PDR rates.[13]

Statistical analysis was performed using the Statistical Package for the Social Sciences software (SPSS 19.0, Chicago, IL, USA). Categorical variables were presented as number of cases and percentages, and were compared using the Pearson's χ^2 test or Fisher's exact test, where appropriate. Continuous variables were expressed as mean ± SD and compared using the non-parametric Mann–Whitney *U*-test and Kruskal–Wallis test, where appropriate. $P < 0.05$ was considered statistically significant.

Results

Characteristics of the study population

A total of 215 HIV-infected patients were enrolled during the inclusion period. Thirty percent of study participants ($n = 64$) were newly diagnosed and ART naive; the remaining 70% ($n = 151$) were ART experienced. Table 1 describes the baseline characteristics of the ART-naive and -experienced groups. In both groups, the majority were female (67.2% in the ART-naive group and 64.9% in the ART-experienced group). The median ages were 34 years (IQR = 32–36) and 40 years (IQR = 38–42) in the ART-naive group and the ART-experienced group, respectively. A lower CD4 count was observed in the ART-naive group compared with the ART-experienced group (225 versus 476 cells/mm^3, $P < 0.001$). The median duration of ART exposure was 48 months (IQR = 15–79). The most commonly used ART regimen in treatment-experienced patients was tenofovir/lamivudine/efavirenz (65.6%), followed by zidovudine/lamivudine/nevirapine (27.2%) and zidovudine/lamivudine/efavirenz (5.3%). Only 2% were on a PI-based regimen that included ritonavir-boosted lopinavir. No patients were on an IN strand transfer inhibitor (INSTI)-based regimen.

HIV genotypic subtypes

Plasma samples were analysed from all 215 patients, and the *pol* region was successfully sequenced (i.e. RT, PR and IN sequences) from 136 patient-derived viruses from 54 ART-naive and 82 ART-experienced patients. The majority were infected with the HIV-1 subtype CRF02_AG (83.1%, 113/136). The subtype distribution for the remaining patients was as follows: subtype G (8.1%, 11/136), subtype C (3.7%, 5/136), subtype CRF09_cpx (2.2%, 3/136), subtype B (1.5%, 2/136), subtype A (0.7%, 1/136) and subtype CRF06_cpx (0.7%, 1/136).

Prevalence of pretreatment DRMs

Genotypic resistance testing was performed in all the ART-naive newly diagnosed patients ($n = 64$). The following sequences were successfully obtained: 49 RT, 44 PR and 42 IN.

Table 1. Baseline characteristics of the study population ($N = 215$)

Characteristic	ART naive, $N = 64$ (100%)	ART experienced, $N = 151$ (100%)	P
Sex, *n* (%)			
male	21 (32.8)	53 (35.1)	NS
female	43 (67.2)	98 (64.9)	NS
Age (years), median (IQR)	34 (32–36)	40 (38–42)	<0.001
CD4 (cells/mm^3), median (IQR)	225 (168–282)	476 (442–510)	<0.001
Duration since diagnosis (months), median (IQR)	0	48 (15–79)	<0.001
ART exposure			
TDF+3TC+EFV	–	99 (65.6)	–
ZDV+3TC+NVP	–	41 (27.2)	–
ZDV+3TC+EFV	–	8 (5.3)	–
TDF+3TC+LPV/r	–	3 (2.0)	–

3TC, lamivudine; EFV, efavirenz; LPV/r, lopinavir/ritonavir; NVP, nevirapine; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine; NS, not significant.

The overall prevalence rate of PDR was 36.7% ($n = 18$): 14.2% to NRTIs and 22.4% to NNRTIs. The most prevalent RT PDR mutations were as follows: K103N ($n = 7$, 14.3%), M184V ($n = 4$, 8.2%) and Y181C ($n = 2$, 4.1%). Other mutations observed with a frequency of 2.0% were as follows: for NRTIs, D67N ($n = 1$), K70R ($n = 1$) and K219E ($n = 1$); and for NNRTIs, V106AM ($n = 1$) and G190A ($n = 1$) (Figure 1). The median number of NRTI and NNRTI resistance-associated mutations (RAMs) was 1 (IQR = 1–3) and 1 (IQR = 1–1), respectively. Four patients (8.2%) harboured both NRTI and NNRTI PDR mutations. No PDR mutations were observed to PIs and only the polymorphism E157Q with minimal effect on INSTI susceptibility was observed in three patients. Based on the GSS estimates, 22.4% ($n = 11$) of patients harboured genotypes that were not susceptible to all three of the component antiretroviral agents in the current recommended first-line regimens in the country (i.e. GSS <3); furthermore, up to 8.2% ($n = 4$) harboured genotypes that were not susceptible to two antiretroviral agents in first-line regimens (Table 2).

Prevalence of RAMs among ART-experienced patients

Genotypic resistance testing was performed in all the ART-experienced patients ($n = 151$), since the VL measurement was not done in individual patients due to inadequate volume of plasma. From the initial 151 patients, 59 RT, 46 PR and 51 IN sequences were obtained. About 64.4% ($n = 38/59$) of ART-experienced patients harboured RAMs to NRTIs and/or NNRTIs. The overall prevalence of NRTI and NNRTI RAMs was 85.2% (52/61) and 96.7% (59/61), respectively. The most prevalent RT RAMs were as follows: K103N ($n = 24$, 40.7%), M184V ($n = 17$, 28.8%), D67N ($n = 9$, 15.3%), T215I/F/Y ($n = 9$, 15.3%) and M41L ($n = 7$, 11.9%) (Figure 1). The median number of NRTI and NNRTI RAMs was 3 (IQR = 1–4) and 2 (IQR = 1–2), respectively. In one patient who was receiving a ritonavir-boosted PI-based regimen, we observed two PI-associated RAMs (M46I and I82A). The mutation L33F was observed in two patients; however, this mutation has minimal impact on PI susceptibility. No RAMs were observed to INSTIs; only the polymorphisms E157Q ($n = 2$), G163KR ($n = 2$) and T97A ($n = 1$) were observed, which have minimal effect on INSTI susceptibility. Of note, there was no significant difference in the median CD4 count when we compared patients with or without RAMs (442 versus 435 cells/mm^3, $P = 0.867$).

Based on GSS estimates, an estimated 56% ($n = 33$) of ART-experienced patients harboured genotypes that were not susceptible to current first-line therapy (Table 2). Furthermore, 30.0% ($n = 18$) of patients will not be fully susceptible to PI- or INSTI-based recommended regimens for rescue therapies; and up to 37.0% ($n = 22$) of patients harboured genotypes already resistant to regimens based on the newer generation of NNRTIs, i.e. etravirine, rilpivirine and doravirine.

Discussion

This cross-sectional study examined the prevalence of DRMs among 64 ART-naive and 151 ART-experienced patients at Connaught Hospital in Freetown, Sierra Leone during November 2017. A high prevalence of PDR mutations (37.0%) was observed to NRTIs and NNRTIs among newly diagnosed ART-naive patients and a high prevalence of RAMs was observed to NRTIs and NNRTIs (>85.0%) in the ART-experienced population. The prevalence of RAMs to PIs was very low or absent. Furthermore, no RAMs were observed to INSTIs. These findings were expected since PI- and INSTI-based regimens are not widely used or are currently unavailable in the country.

To the best of our knowledge, this study is the first to report on the prevalence of HIVDR in Sierra Leone. As indicated earlier, HIVDR has been a growing public health problem in West Africa in recent years[8–12] and is likely to have been further exacerbated by the considerable disruptions in HIV services in Sierra Leone, Guinea and Liberia (the three most affected countries) during the Ebola epidemic of 2014–16.[14] Two earlier studies by Loubet *et al.*[9,15] conducted in neighbouring Liberia just before the onset of the Ebola epidemic (2013) had found a PDR prevalence rate of 5.7% in ART-naive patients ($n = 116$)[15] and RAM prevalences of 63% and 71% to NRTIs and NNRTIs, respectively, in ART-experienced patients ($n = 90$).[9] Thus, our study provides the first major update on HIVDR in the three most affected countries in the immediate post-Ebola period. Compared with the two pre-Ebola era studies from Liberia,

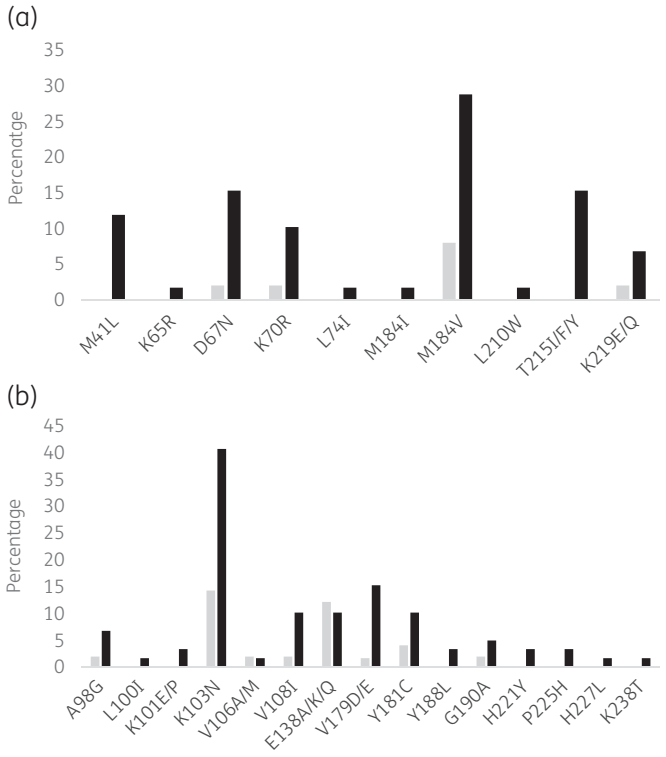

Figure 1. Prevalence of HIV-1 DRMs. (a) NRTI RAMs. The overall prevalence of HIVDR to NRTIs was 14.2% in ART-naive patients and 85.2% in ART-experienced patients. (b) NNRTI RAMs. The overall prevalence of RAMs to NNRTIs was 22.4% in ART-naive patients and 96.7% in ART-experienced patients. Grey bars, ART naive; black bars, ART experienced.

we observed a much higher prevalence of RAMs to NRTIs and NNRTIs in ART-naive and -experienced patients in our cohort of patients from Sierra Leone.

Baseline PDR testing is recommended as part of the initial evaluation of newly diagnosed HIV patients by current international treatment guidelines by the US Department of Health and Human Services,[5] the European AIDS Clinical Society,[16] the Spanish AIDS Study Group (GESIDA)[17] and the International Antiviral Society-USA Panel.[18] PDR testing has been found to be cost-effective and beneficial in terms of gain in quality-adjusted life years (QALYs) when PDR prevalence is >1%, especially when considering using an NNRTI-containing regimen as first-line therapy.[19] Given our findings, baseline PDR testing should be considered in the routine care of HIV-infected patients in Sierra Leone, but remains a major challenge due to the lack of resources and expertise to undertake routine HIVDR testing in the country.

We observed a high prevalence of RAMs among ART-experienced patients, which significantly increases the probability of virological failure and onward transmission of HIV drug-resistant strains in the general population. The WHO defines virological failure as plasma VL >1000 copies/mL based on two consecutive VL measurements after 3 months, with adherence support.[7] Since VL testing is not widely available in most resource-limited settings such as Sierra Leone, identifying patients in virological failure can be challenging. More commonly, CD4 cell count and clinical monitoring are used to assess for treatment failure. Interestingly, we did not observe any significant difference in the median CD4 cell count of participants who harboured at least one RAM versus those who did not have any (442 versus 435 cells/mm^3, $P = 0.867$). This finding suggests that CD4 monitoring alone may be an adequate means of assessing virological failure in patients in Sierra Leone.

Table 2. Prevalence of HIV-1 drug resistance genotypes to first-, second- and third-line ART in Sierra Leone based on the GSS estimates

Characteristic	First-line ART	GSS <3, *n* (%)	Second- and third-line ART		GSS <3, *n* (%)
ART naive	TDF+3TC+EFV	11 (22.4)	2 NRTIs+PI	TDF+FTC+DRV/r	4 (9.5)
	ZDV+3TC+NVP	11 (22.4)		TDF+3TC+LPV/r	4 (9.5)
			2 NRTIs+INSTI	TDF+FTC+RAL	4 (9.5)
				TDF+FTC+DTG	4 (9.5)
				TDF+FTC+EVG/c	4 (9.5)
				TDF+FTC+BIC	4 (9.5)
			2 NRTIs+NNRTI	TDF+FTC+RPV	9 (18.3)
				TDF+3TC+ETV	5 (10.2)
				TDF+3TC+DVR	7 (14.3)
ART experienced	TDF+3TC+EFV	33 (56.0)	2 NRTIs+PI	TDF+FTC+DRV/r	18 (30.5)
	ZDV+3TC+NVP	33 (56.0)		TDF+3TC+LPV/r	18 (30.5)
			2 NRTIs+INSTI	TDF+FTC+RAL	18 (30.5)
				TDF+FTC+DTG	18 (30.5)
				TDF+FTC+EVG/c	18 (30.5)
				TDF+FTC+BIC	18 (30.5)
			2 NRTIs+NNRTI	TDF+FTC+RPV	22 (37.0)
				TDF+3TC+ETV	22 (37.0)
				TDF+3TC+DVR	22 (37.0)

3TC, lamivudine; BIC, bictegravir; DRV/r, darunavir/ritonavir; DTG, dolutegravir; DVR, doravirine; EFV, efavirenz; ETV, etravirine; FTC, emtricitabine; EVG/c, elvitegravir/cobicistat; LPV/r, lopinavir/ritonavir; NVP, nevirapine; RAL, raltegravir; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine.

Based on the GSS estimates, 22.4% of the ART-naive patients and 56.0% of the ART-experienced patients exhibited resistance to the currently recommended first-line therapy in Sierra Leone (Table 2). Furthermore, 30.0% of the ART-experienced patients had genotypes that were not fully susceptible to PI- or INSTI-based regimens, while up to 37.0% were not susceptible to the newer generation NNRTI-based regimens. These estimates would suggest that the options for rescue therapy for patients failing first-line ART in Sierra Leone are extremely limited as newer generation NNRTIs are in short supply, while INSTIs are currently unavailable. However, all three patients on boosted lopinavir-based therapy in this study did not exhibit any meaningful PI RAMS. Interestingly, Jespersen *et al*.[20] recently showed similar rates of viral suppression, adverse clinical events and mortality in an ITT analysis that randomized 400 HIV-infected patients from the Bissau HIV cohort to first-line NNTRI- and PI (lopinavir/ritonavir)-based treatment arms. Similar to our study, Jespersen *et al*.[20] did not detect any PI RAMs; rather they found high resistance levels to NNRTIs (56.7%). Currently, boosted lopinavir remains the only available PI in Sierra Leone as first-line ART and could presumably serve as a viable rescue option for patients failing NNRTI-based first-line therapy in the country.

The majority of our study participants were infected with the recombinant HIV-1 subtype CRF02_AG (83.1%), with other minority variants making up <17.0%. These findings are in concordance with several studies from the West Africa region.[8–12] Thus far, the molecular epidemiology of the circulating HIV strains in Sierra Leone has been limited to a few case reports mainly of HIV-infected Sierra Leonean migrants in Europe and North America.[21–25] Interestingly, although HIV-2 is endemic in Sierra Leone and other West African countries, we did not detect any HIV-2-mono-infected or HIV-1/2 dually infected cases in our cohort. Susceptibility to ART may be influenced by the genetic diversity of HIV subtypes and recombinant forms.[26,27] Thus, a more detailed study is needed to characterize the epidemiology of circulating HIV strains and their potential influence on choice of ART in the clinical management of HIV-infected patients in Sierra Leone.

Our study had several limitations, including the small sample size and its restriction to a single study site, making our findings not readily generalizable. Additionally, VL measurement was not performed to assess virological failure due to insufficient volume of plasma samples. Other limitations included inability to ascertain adherence to ART and its potential role in the development of DRMs in our cohort. Finally, we could not exclude the possibility that some of the female participants may have previously been exposed to ART through the prevention of mother-to-child transmission ('PMTCT') programme or the possibility that some of the newly HIV diagnosed patients in the study may have previously been diagnosed elsewhere and received ART—a common occurrence in many resource-limited settings. Notwithstanding, we believe that this study merits attention because it offers the first critical insight into a public problem of growing magnitude and importance in Sierra Leone.

Conclusions

In summary, a high prevalence of circulating NRTI and NNRTI resistance variants was observed in both ART-naive and -experienced HIV-1-infected patients in Sierra Leone. These findings underscore the urgent need for the implementation of surveillance programmes for HIVDR, as well as routine VL and drug resistance testing in the clinical management of patients in this country. Larger studies are needed to help to inform the establishment of national guidelines for ART and the clinical monitoring of HIV-infected patients in Sierra Leone.

Acknowledgements

We acknowledge the HIV patients of Sierra Leone who made this work possible and we dedicate this paper to the evergreen memory of the late Charles Saa Yendewa (1936–2006)—father, teacher and gentleman.

Funding

This work was supported in part by grants from NIH NIAID T32 AI07024 Training in Geographic Medicine and Infectious Diseases 2017, School of Medicine, Case Western Reserve University (G. A. Y.), the Roe Green Travel Medicine Award 2017, University Hospitals Cleveland Medical Center (G. A. Y.), Instituto de Salud Carlos III and Fondo Europeo de Desarrollo Regional-FEDER, Red Española de Investigación en SIDA (RD16/0025/0026) (E. P.), Xunta Galicia-Fondo Social Europeo (IN606A-2016/023) (E. P.) and Fundación Biomédica Galicia Sur (E. P.).

Transparency declarations

None to declare.

Author contributions

G. A. Y., F. S., R. A. S. and E. P. conceptualized the study. G. A. Y., F. S., S. L., G. F. D. and M. S. obtained the clinical specimens and recorded the clinical and demographic data. M. R., L. P., A. T. and E. P. conducted the assays. G. A. Y., M. R., L. P., A. T., R. A. S. and E. P. analysed and interpreted the data. G. A. Y., R. A. S. and E. P. drafted the manuscript. All authors edited and approved the final version of the manuscript.

References

1 World Bank. *Data Sierra Leone*. 2016. http://www.worldbank.org/en/country/sierraleone.

2 UNAIDS. *Country Sierra Leone 2016*. 2016. http://www.unaids.org/en/regionscountries/countries/sierraleone.

3 National HIV/AIDS Secretariat. *National Strategic Plan 2016–2020*. 2015. http://www.nas.gov.sl/images/stories/publications/SierraLeoneNationalStrategicPlan2016-2020.pdf.

4 National HIV/AIDS Secretariat. *Sierra Leone ARV Guidelines August 2006*. 2006. http://www.nas.gov.sl/images/stories/publications/Sierra%20Leone%20ARV%20Guidelines%20August%202006.pdf.

5 Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*. Department of Health and Human Services. https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf.

6 WHO. *Antiretroviral Treatment as Prevention (TasP) of HIV and TB: 2012 Update*. 2012. http://apps.who.int/iris/bitstream/10665/70904/1/WHO_HIV_2012.12_eng.pdf.

7 WHO. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach—Second Edition*. 2016. http://apps.who.int/iris/bitstream/handle/10665/208825/9789241549684_eng.pdf?sequence=1.

8 WHO. *HIV Drug Resistance Report 2017*. 2017. http://apps.who.int/iris/bitstream/handle/10665/255896/9789241512831-eng.pdf?sequence=1.

9 Loubet P, Charpentier C, Visseaux B *et al*. Prevalence of HIV-1 drug resistance among patients failing first-line ART in Monrovia, Liberia: a cross-sectional study. *J Antimicrob Chemother* 2015; **70**: 1881–4.

10 Diouara AA, Ndiaye HD, Guindo I *et al*. Antiretroviral treatment outcome in HIV-1-infected patients routinely followed up in capital cities and remote areas of Senegal, Mali and Guinea-Conakry. *J Int AIDS Soc* 2014; **17**: 19315.

11 Chaplin B, Akanmu AS, Inzaule SC *et al*. Association between HIV-1 subtype and drug resistance in Nigerian infants. *J Antimicrob Chemother* 2019; **74**: 172–6.

12 Jespersen S, Tolstrup M, Hønge BL *et al*. Bissau HIV cohort study group. High level of HIV-1 drug resistance among patients with HIV-1 and HIV-1/2 dual infections in Guinea-Bissau. *Virol J* 2015; **12**: 41.

13 Bennett DE, Camacho RJ, Otelea D *et al*. Drug resistance mutations for surveillance of transmitted HIV-1 drug-resistance: 2009 update. *PLoS One* 2009; **4**: e4724.

14 Parpia AS, Ndeffo-Mbah ML, Wenzel NS *et al*. Effects of response to 2014–2015 Ebola outbreak on deaths from malaria, HIV/AIDS, and tuberculosis, West Africa. *Emerg Infect Dis* 2016; **22**: 433–41.

15 Loubet P, Charpentier C, Visseaux B *et al*. Short communication: prevalence of HIV-1 transmitted drug resistance in Liberia. *AIDS Res Hum Retroviruses* 2014; **30**: 863–6.

16 European AIDS Clinical Society. *EACS Guidelines Version 9.0 October 2017*. 2017. http://www.eacsociety.org/files/guidelines_9.0-english.pdf.

17 GESIDA. *Documento de consenso de Gesida/Plan Nacional sobre el SIDA respecto al tratamiento antiretroviral en adultos infectados por el virus de la inmunodeficiencia humana. Updated January 2018*. 2018. http://gesida-seimc.org/wcontent/uploads/2018/01/gesida_TAR_Gesida_y_PNS_2018.pdf.

18 Saag MS, Benson CA, Gandhi RT *et al*. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel. *JAMA* 2018; **320**: 379–96.

19 Sax PE, Islam R, Walensky RP *et al*. Should resistance testing be performed for treatment-naive HIV-infected patients? A cost-effectiveness analysis. *Clin Infect Dis* 2005; **41**: 1316–23.

20 Jespersen S, Hønge BL, Krarup H *et al*. Protease inhibitors or NNRTIs as first-line HIV-1 treatment in West Africa (PIONA): a randomized controlled trial. *J Acquir Immune Defic Syndr* 2018; **79**: 386–93.

21 Hamers RL, Wensing AM, Back NK *et al*. Multi-nucleoside reverse transcriptase inhibitor resistant HIV type-1 in a patient from Sierra Leone failing stavudine, lamivudine and nevirapine. *Antivir Ther* 2011; **16**: 115–8.

22 Lospitao E, Alvarez A, Soriano V *et al*. HIV-1 subtypes in Spain: a retrospective analysis from 1995 to 2003. *HIV Med* 2005; **6**: 313–20.

23 Davanos N, Panos G, Gogos CA *et al*. HIV-1 subtype characteristics of infected persons living in southwestern Greece. *HIV AIDS (Auckl)* 2015; **7**: 277–83.

24 Paraskevis D, Magiorkinis E, Magiorkinis G *et al*. Molecular characterization of a complex, recombinant human immunodeficiency virus type 1 (HIV-1) isolate (A/G/J/K/?): evidence to support the existence of a novel HIV-1 subtype. *J Gen Virol* 2001; **82**: 2509–14.

25 Yendewa GA, Poveda E, Yendewa SA *et al*. HIV/AIDS in Sierra Leone: characterizing the hidden epidemic. *AIDS Rev* 2018; **20**: 104–13.

26 Wainberg MA, Brenner BG. The impact of HIV genetic polymorphisms and subtype differences on the occurrence of resistance to antiretroviral drugs. *Mol Biol Int* 2012; **12**: 256982.

27 Lessells RJ, Katzenstein DK, de Oliveira T. Are subtype differences important in HIV drug resistance? *Curr Opin Virol* 2012; **2**: 636–43.