Short Report on HIV Drug Resistance: Survey Among People at Risk for HIV in Unguja Zanzibar, Tanzania, 2023

Background

Zanzibar is a semi-autonomous region of Tanzania, comprised of islands off the coast of mainland Tanzania. The two main islands are Unguja and Pemba, with the majority of the population residing on Unguja. Results from the Tanzania HIV Impact Survey (THIS) 2022–2023 found the prevalence of HIV infection in Zanzibar was low (less than 0.5%) in the general population. Routine surveillance among key populations (KPs) in Zanzibar has shown disproportionately high HIV prevalence (over 5%) among people who inject drugs (PWID), men who have sex with men (MSM), and Women who engage in commercial sex (WECS). The Zanzibar Integrated HIV, Hepatitis, Tuberculosis, and Leprosy Programme (ZIHHTLP) in the Ministry of Health implemented a bio-behavioral survey (BBS) among KPs between July and September 2023 in Unguja, Zanzibar, Tanzania. This was the fourth survey among these populations, with similar surveys conducted in 2019, 2012, and 2007.This drug resistance report serves as an additional component of the main Zanzibar IBBS 2023 report after the HIV drug resistance (HIVDR) testing results were released from the testing laboratory.

The survey was conducted by ZIHHTLP with funding from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and technical assistance provided by the University of California, San Francisco and the U.S. Centers for Disease Control and Prevention (CDC).

Methodology

We performed HIV drug resistance testing to all participants who had a reactive HIV result on both SD Bioline and Unigold and a viral load result of >200 copies/mL. Raw chromatogram data (ab1 files) were received from Temeke Specialised Laboratory (TSL), which included 42 sequences covering the protease and reverse transcriptase (PR/RT) region and 60 sequences covering the integrase (IN) region. The chromatogram data were analysed using RECall (v2.35.1) —a web-based sequence analysis tool. Raw chromatograms were reviewed manually, and edits were made based on the quality of the base chromatogram. Edits were only made to the drug resistance mutation positions if that position was supported by at least two primers from the forward primer and reverse primers. Consensus sequences were downloaded and then subjected to multiple sequence alignment using the AUGUR tool, which utilises Mafft. The sequences were aligned to the standard references for both regions (PR/RT and IN). This was done to detect any insertions or deletions in the sequences relative to the reference sequences. Then the sequences were subjected to quality control (QC) analysis using the WHO HIVDR QC analysis tool, Version v2.34. Quality of the sequences were evaluated based on the criteria as described in the Sequence Quality Assurance (QA) Standard Operating Proceedure (SOP) Annex in the updated Laboratory Network Operational Framework document. At this stage issues related Apolipoprotein B mRNA Editing Catalytic polypeptide-like enzymes (APOBEC) mutations, unusual mutations, premature stop codons, frameshifts (bad insertions and deletions), sample contamination due to known laboratory strains or between samples are reviewed. The samples that passed the QC check were submitted to the Stanford HIVDR database for further quality checking and prediction of drug

resistance profiles. For HIV-1 subtyping, sequences of the PR/RT region were used in the REGA HIV-1 subtyping tool (V.2.46). The maximum phylogenetic tree was created using IQ-TREE 2 with 1000 bootstraps, model selection based on the Bayesian information criterion (BIC).

Results

Out of 42 sequences, 31 sequences in the PR/RT region progressed to the QC stage, and of 60 sequences in the IN region, 35 progressed. This resulted in 19 sequences that had both the PR/RT and the IN region, 12 sequences in the PR/RT regions only, and 16 sequences in the IN region only. The results presented are based on the 28 HIVDR sequences from this survey.

Of the available sequences, 15 were complete sequences allowing for comprehensive resistance assessment, while 13 provided partial results for specific antiretroviral therapy (ART) classes. Overall, seven participants had evidence of major drug resistance. Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance was most frequent (5/7), followed by nucleoside reverse transcriptase inhibitor (NRTI) resistance (2/7). No major protease inhibitor (PI) or integrase strand transfer inhibitor (INSTI) resistance was detected, although one case demonstrated low-level dolutegravir (DTG) resistance (Table 1).

Major drug resistance by population

By population, WECS had the highest burden of major resistance 50% (5/10), followed by MSM 33% (4/12) and PWID 16% (1/6) (Figure 1).

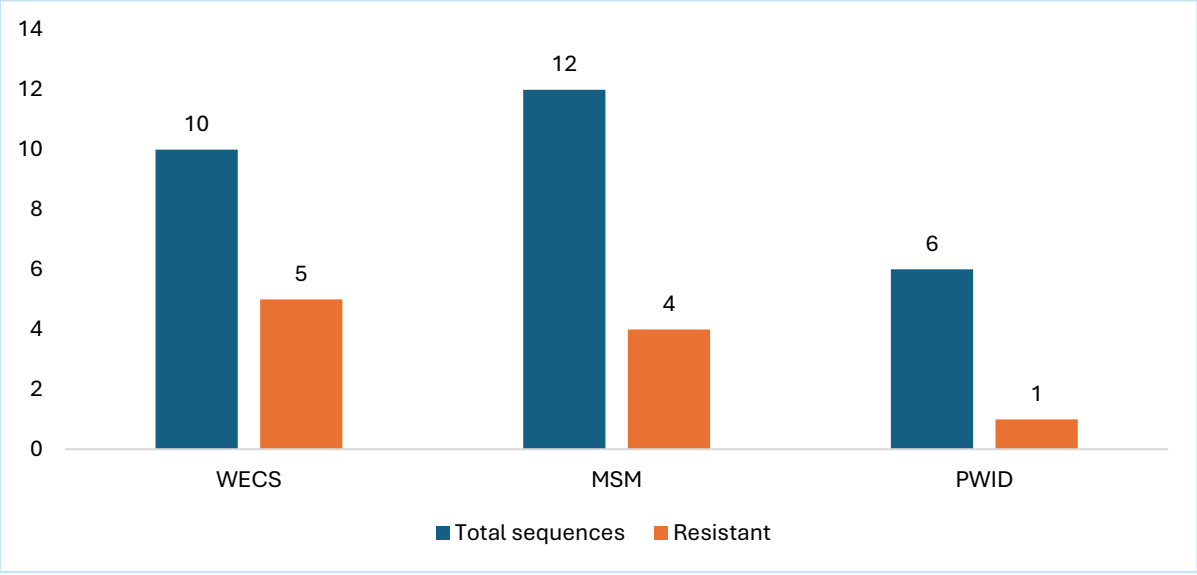

Figure 1. Prevalence of ART Resistance, Survey Among People at Risk for HIV in Unguja Zanzibar, Tanzania, 2023

Table 1: HIV Resistance Profiles of Antiretroviral Groups, Survey Among People at Risk for HIV in Unguja Zanzibar, Tanzania, 2023

	Resistance Classification	Total Sequences	Resistant
		N	n [1]
Total			
Overall (N=28)	Major[2] INSTI[3] Resistance	15	0
	Low, intermediate or high DTG Resistance[4]	15	1
	Major PI[5] Resistance	15	0
	Major NRTI[6] Resistance	15	2
	Major NNRTI[7] Resistance	15	5
	Any Major Drug Resistance	28	10
Population			
PWID[8] (N=6)	Major INSTI Resistance	1	0
	Low, intermediate or high DTG Resistance	1	0
	Major PI Resistance	1	0
	Major NRTI Resistance	1	0
	Major NNRTI Resistance	1	0
	Any Major Drug Resistance	6	1
WECS[9] (N=10)	Major INSTI Resistance	6	0
	Low, intermediate or high DTG Resistance	6	1
	Major PI Resistance	6	0
	Major NRTI Resistance	6	3
	Major NNRTI Resistance	6	4
	Any Major Drug Resistance	10	5
MSM[10] (N=12)	Major INSTI Resistance	9	0
	Low, intermediate or high DTG Resistance	9	0
	Major PI Resistance	9	0
	Major NRTI Resistance	9	1
	Major NNRTI Resistance	9	4
	Any Major Drug Resistance	12	4

Note: [1]corresponds to unweighted numbers and percentages; [2]corresponds to high level resistance (level 5 by Stanford database); [3]included Bictegravir, Cabotegravir, Dolutegravir, Elvitegravir, Raltegravir; [4]corresponds to levels 3–5 by Stanford database; [5]included Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Saquinavir, Tipranavir; [6]includes Abacavir, Zidovudine, Stavudine, Emtricitabine, Lamivudine, Tenofovir; [7]Doravirine, Efavirenz, Etravirine, Nevirapine, Rilpivirine; [8]PWID stands for people who inject drugs; [9]WECS stands for engaged in commercial sex, [10]MSM stands for men who have sex with men.

Major drug resistance by self-reported ART history

Of the 28 participants whose samples were tested, 21 (75%) self-reported never had been on ART. Among these, six (29%) had major resistance mutations. Among the seven participants with prior ART exposure, six had been on ART for more than six months, of whom three (50%) were found to have major resistance mutations. The remaining participant, who had initiated ART within the last six months, was also found to have major resistance mutations.

Effectiveness of individual antiretroviral drugs

INSTIs remained highly effective, with only a single sequence demonstrating reduced susceptibility to multiple agents, including dolutegravir (DTG), bictegravir (BIC), cabotegravir (CAB), elvitegravir (EVG), and raltegravir (RAL). PIs exhibited complete susceptibility across all drugs assessed.

Table 2: HIV Antiretroviral Resistance Profiles by Standford Database Susceptibility Categories, Survey Among People at Risk for HIV in Unguja Zanzibar, Tanzania, 2023

Drug	Total Sequences	Susceptible[1]	Low [2]	Intermediate[3]	High[4]
	N	n [5]	n	n	n
NRTIs[6]					
ABC	15	15	0	0	0
AZT	15	14	1	0	0
D4T	15	14	1	0	0
FTC	15	15	0	0	0
3TC	15	15	0	0	0
TDF	15	15	0	0	0
DDL	15	14	1		
DPV	15	12	3	0	0
NNRTIs[7]					
DOR	15	14	1	0	0
EFV	15	13	1	0	1
ETR	15	12	3	0	0
NVP	15	13	1	0	1
RPV	15	12	3	0	0
PIs[8]					
ATV	14	14	0	0	0
DRV	14	14	0	0	0
FPV	14	14	0	0	0
IDV	14	14	0	0	0
LPV	14	14	0	0	0
NFV	14	13	1	0	0
SQV	14	14	0	0	0

TPV	14	13	1	0	0
INSTIs[9]					
BIC	15	14	1	0	0
CAB	15	14	1	0	0
DTG	15	14	1	0	0
EVG	15	14	1	0	0
RAL	15	14	1	0	0

Note: [1]correspond to levels 1–2 in Stanford database; [2]correspond to level 3 in Stanford database; [3]correspond to level 4 in Stanford database; [4]correspond to level 5 in Stanford database; [5]correspond to unweighted numbers and percentages; [6]correspond to nucleoside reserve transcriptase inhibitors including Abacavir (ABC), Zidovudine (AZT), Stavudine (D4T), Didanosine(DDL),Emtricitabine (FTC), Lamivudine (3TC), Tenofovir (TDF); [7]correspond to non-nucleoside reverse transcriptase inhibitors including Doravirine (DOR), Dapivirine(DPV), Efavirenz (EFV), Etravirine (ETR), Nevirapine (NVP), Rilpivirine (RPV); [8]correspond to protease inhibitors including Atazanavir (ATV), Darunavir (DRV), Fosamprenavir (FPV), Indinavir (IDV), Lopinavir (LPV), Nelfinavir (NFV), Saquinavir (SQV), Tipranavir (TPV); [9]correspond to integrase stand transfer inhibitors including Bictegravir (BIC), Cabotegravir (CAB), Dolutegravir (DTG), Elvitegravir (EVG), Raltegravir (RAL).

Drug Resistance Implications and Conclusion

DTG-based and PI-based regimens remain effective in Zanzibar. The high prevalence of NNRTI resistance, particularly among WECS, may reflect suboptimal adherence among individuals previously treated with NNRTI-based regimens or transmission of resistant HIV strains. Sustained adherence support, routine viral load monitoring, and timely regimen switching upon treatment failure are critical for maintaining ART effectiveness in people at risk for HIV.