ARV DRUG USE AND HIV DRUG RESISTANCE AMONG YOUNG WOMEN IN SOUTH AFRICA (HPTN 068)

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BACKGROUND

Antiretroviral (ARV) drugs are widely used for HIV treatment and prevention, and may be used for other reasons in some populations. We analyzed ARV drug use and HIV drug resistance among young women enrolled in the HIV Prevention Trials Network (HPTN) 068 study. Young women in sub-Saharan Africa have significantly higher rates of HIV infection and acquire HIV infection at a younger age than their male peers. HPTN 068 was conducted in rural northeast South Africa and evaluated the impact of cash transfer on HIV incidence conditional on high school attendance (study period: 2011-2015).

METHODS

STUDY COHORT

In HPTN 068 (main study), young women were enrolled in high school and were tested for HIV infection annually until their expected graduation date. Some participants had one additional post-graduation follow-up visit after exiting from the main study (follow-up study).

In this study, we analyzed two sample sets:

(1) Enrollment samples (2,526 women: 80 HIV infected; 2,446 HIV uninfected)

(2) Samples from the first HIV-positive visit (162 seroconverters; 107 in the main study, 55 in the follow-up study)

ARV DRUG TESTING

ARV drug testing was performed using a qualitative assay based on high-performance liquid chromatography coupled with high-resolution accurate-mass mass spectrometry. This assay detects 20 ARV drugs from five drug classes:

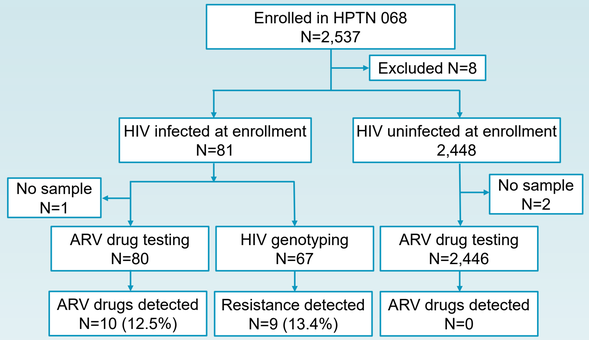
- Nine protease inhibitors (PIs)
- Six nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)
- Three non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- One CCR5 receptor antagonist
- One integrase strand transfer inhibitor

HIV DRUG RESISTANCE TESTING

HIV genotyping was performed using the ViroSeq HIV-1 Genotyping System v2.8 (Abbott Molecular, Des Plaines, IL) for samples with HIV viral loads >400 copies/mL.

RESULTS

Figure 1. Detection of ARV drugs and HIV drug resistance in women at study enrollment.



ARV drug testing was performed using enrollment samples from 2,526 women (Figure 1). ARV drugs were detected in 10 (12.5%) of 80 samples from women who were HIV-infected at enrollment (Table 1). Six samples had one NNRTI with one or two NRTIs detected, three samples had one NNRTI alone, one sample had one NRTI alone. No ARV drugs were detected in samples from the 2,446 women who were HIV uninfected at enrollment.

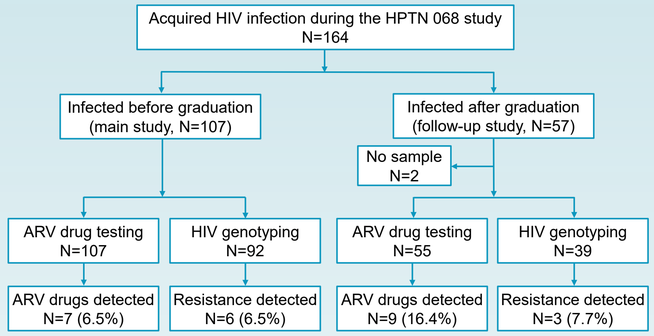
HIV drug resistance mutations were detected in 9 of 67 women who were HIV-infected at enrollment. ARV drugs were detected in 5 of those samples (Table 1).

Table 1. ARV drugs and HIV drug resistance in HIV-infected women at study enrollment.

Status	Study visit	Viral load	ARV drugs detected		Mutations detected	
			NNRTI	NRTI	NNRTI	NRTI
HIV infected at Enrollment (ARV drugs detected)	Enrollment	68	EFV	3TC, TFV	--	--
	Enrollment	<40	NVP	3TC, TFV	--	--
	Enrollment	<40	NVP	3TC, ZDV	--	--
	Enrollment	<40	EFV	3TC	--	--
	Enrollment	<40	EFV	3TC	--	--
	Enrollment	9,968	NVP	3TC	Y181C, G190A	M184V
	Enrollment	164,089	EFV	None	K103N	M184V
	Enrollment	388,773	EFV	None	K103N	M184V
	Enrollment	7,425	NVP	None	K103N, Y181C	M184V
	Enrollment	36,062	None	3TC	V106M	M184I/V
HIV infected at Enrollment (no drugs detected)	Enrollment	119,267	None	None	K103N	--
	Enrollment	73,392	None	None	V106M	--
	Enrollment	1,263	None	None	Y181C	--
	Enrollment	15,225	None	None	G190A	--

Abbreviations: NNRTI; non-nucleoside/nucleotide reverse transcriptase inhibitor; NRTI: nucleoside/nucleotide reverse transcriptase inhibitor; EFV: efavirenz; NVP: nevirapine; 3TC: lamivudine; FTC: Emtricitabine; TFV: tenofovir.

Figure 2. Detection of ARV drugs and HIV resistance testing in seroconverters.



None of the 164 seroconverters had drugs detected at enrollment (before HIV infection). ARV drugs were detected in 16 (9.9%) of 162 samples from the first HIV-positive visit (Figure 2); all 16 samples had EFV; 14 samples also had one or two NRTIs (Table 2). Major resistance mutations were detected in 9 (5.6%) of the 162 seroconverter samples. ARV drugs were detected in one of those samples (Table 2).

Table 2. ARV drugs and HIV drug resistance in seroconverters.

Status	Study visit	Viral load	ARV drugs detected		Mutations detected	
			NNRTI	NRTI	NNRTI	NRTI
HIV infected after enrollment (ARV drugs detected)	Year 1	<40	EFV	TFV, 3TC	--	--
	Year 1	475	EFV	TFV, 3TC	No sample	No sample
	Year 1	56	EFV	TFV, 3TC	--	--
	Year 1	4,188	EFV	TFV, FTC	--	--
	Year 2	137	EFV	None	--	--
	Year 3	207	EFV	TFV, FTC	--	--
	Graduation	<40	EFV	TFV, 3TC	--	--
	Post-Grad	766	EFV	TFV, FTC	K103N	--
	Post-Grad	181	EFV	TFV, FTC	--	--
	Post-Grad	71	EFV	TFV, FTC	--	--
	Post-Grad	<40	EFV	TFV, FTC	--	--
	Post-Grad	<40	EFV	TFV, FTC	--	--
	Post-Grad	<40	EFV	TFV, FTC	--	--
	Post-Grad	<40	EFV	FTC	--	--
	Post-Grad	<40	EFV	FTC	--	--
	Post-Grad	85	EFV	None	--	--
HIV infected after enrollment (no drugs detected)	Year 1	22,247	None	None	K103N	--
	Year 2	3,664	None	None	K103N	--
	Year 2	8,860	None	None	Y181C	
	Year 3	10,159	None	None	K103N	--
	Year 3	94,359	None	None	K103N	--
	Graduation	91,235	None	None	V106M	--
	Post-grad	11,872	None	None	K103N	--
	Post-grad	50,037	None	None	K103N	--

The association of demographic, laboratory, and clinical factors with detection of ARV drugs and HIV drug resistance was examined; factors included age, viral load, CD4 cell count, infection group, pregnancy history, food insecurity, school attendance, depression, alcohol use, and orphanhood.

- ARV drugs was detected more frequently in women who had a lower viral load at their first HIV-positive visit ($p<0.0001$).
- ARV drugs were also detected more frequently in women who had two deceased parents (double orphans) compared to those had two living parents (27.8% vs. 10.5%, $p=0.04$).

The only factor associated with HIV drug resistance was having one parent deceased, compared to having two living parents ($p=0.04$). The proportion of women who had viral loads <400 copies/mL (below the cutoff for genotyping) was similar for those with two living parents vs. one or no living parents ($p=0.45$).

CONCLUSIONS

ARV drug use was not detected among HIV-uninfected women in this cohort from rural South Africa.

ARV drug use was relatively infrequent among women with prevalent infection (12/5%) and incident infection (9.9%).

Among the women who were using ARV drugs, many were not virally suppressed and many had HIV drug resistance; this suggests a need for broader HIV/AIDS education and ART counseling in the study communities.

It was not possible to determine if the low rate of ARV drug use in this cohort reflected lack of knowledge of HIV status or other factors.

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