HIGH HIV-1 DIVERSITY AND MODERATE PREVALENCE OF TRANSMITTED DRUG RESISTANCE MUTATIONS AMONG ARV-NAIVE HIV-INFECTED PREGNANT WOMEN IN RIO DE JANEIRO, BRAZIL

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Introduction

- The increase in the access of antiretroviral (ARV) drugs in Brazil has strong impact in the reduction of morbidity and mortality of HIV-1 positive individuals.
- However, it may also favors the emergence of HIV-1 drug-resistant variants, due to low genetic barrier of some drugs, poor adhesion to treatment regimens, among others.
- These variants may limit the therapeutic options available for people who were newly infected with them.

Material and methods

- The viral RNA was extracted from 51 plasma samples obtained from pregnant ARV-naïve patients.
- The HIV-1 protease and reverse transcriptase (PR/RT) regions of the *pol* gene were sequenced using an in house genotyping method.
- HIV-1 subtypes were determined by phylogenetic and bootscanning analyzes.
- TDRM were detected using the Calibrated Population Resistance Tool-CPR v.6.0.

Results

- The HIV-1 subtype B was identified in 64.5% of the sequences, representing a decrease in the prevalence found in the previous period (81%).
- The frequencies of the subtypes F1 (9.8%) and C (3.9%) remained similar, while there was a 2.5-times increase in the recombinant forms frequency (from 8.0% to 21.8%) since the previous study.
- The overall prevalence of any HIV-1 TDRM was higher (13.7%) than the previous estimate (10.7%).
- TDRM for protease and non-nucleoside reverse transcriptase inhibitors increased from 3.0% to 7.5% and 2.0% to 3.9%, respectively.
- A prevalence of 1.9% of TDRM for nucleoside reverse transcriptase inhibitors was identified in the analyzed samples collected between 2012 to 2013, contrasting with the 5.6%-prevalence previously found.

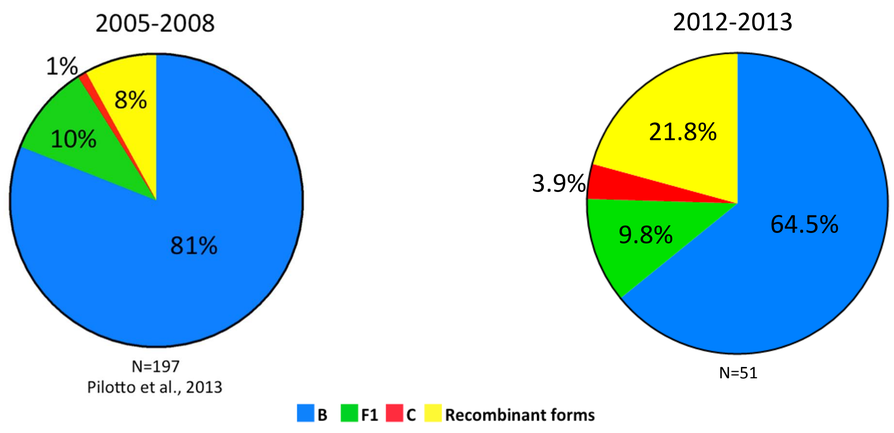

Figure 1. Prevalence of HIV-1 subtypes found in the two time intervals.

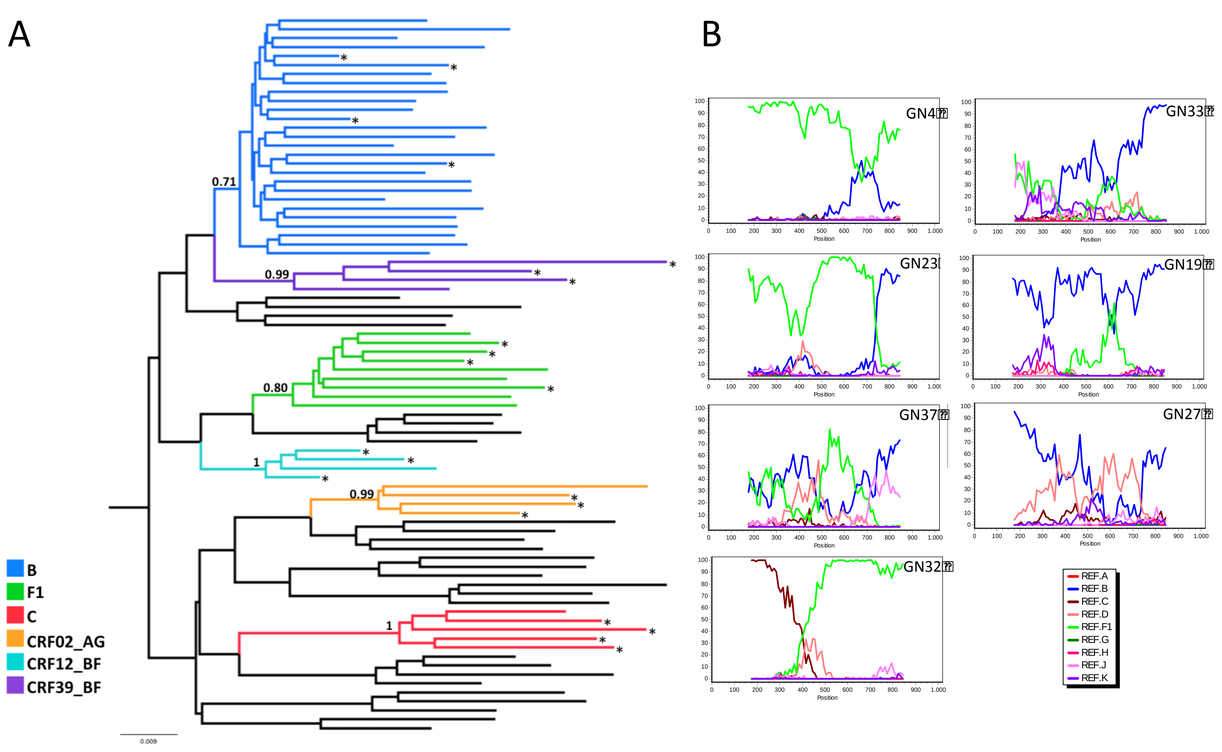

Figure 2. Subtype classification of sequences. A) NJ tree of PR/RT region (~1,000 pb). HIV-1 reference sequences of pure subtypes and some CRFs (A-D, F-G, H, J, CRF02_AG, CRF12_BF e CRF39_BF) were included and marked with asterisks or colored black. Bootstrap support values were displayed at key nodes. Clades representing the subtypes and CRFs found were colored according to the legend. Horizontal branch lengths are drawn to scale with the bar at the bottom indicating nucleotide substitutions per site. B) Bootscanning analysis of the URFs found. The parameters used were a window of 300nt, step of 10nt and 100 resamplings. The color of lines represents the subtypes according to the legend.

Table 1. TDRM prevalence present in the two time periods.

ARV classes	TDRM prevalence	
	2005-2008*	2012-2013
Global	10.7%	13.7%
PI	3%	7.5%
NRTI	5.6%	1.9%
NNRTI	2%	3.9%

* Pilotto et al., 2013

Table 2. Protease inhibitor, nucleoside reverse transcriptase inhibitor, and non-nucleoside, reverse transcriptase inhibitor transmitted drug resistance mutations according to subtypes

Sample ID	PI	NRTI	NNRTI	Subtype
GN11	M46I	None	None	B
GN20	M46L	None	None	B
GN50	M46L	None	None	B
GN33	D30N, N88D	None	None	B
GN49	None	D67N, K219Q	None	B
GN14	None	None	K101E, G190A	F1
GN31	None	None	G190A	F1

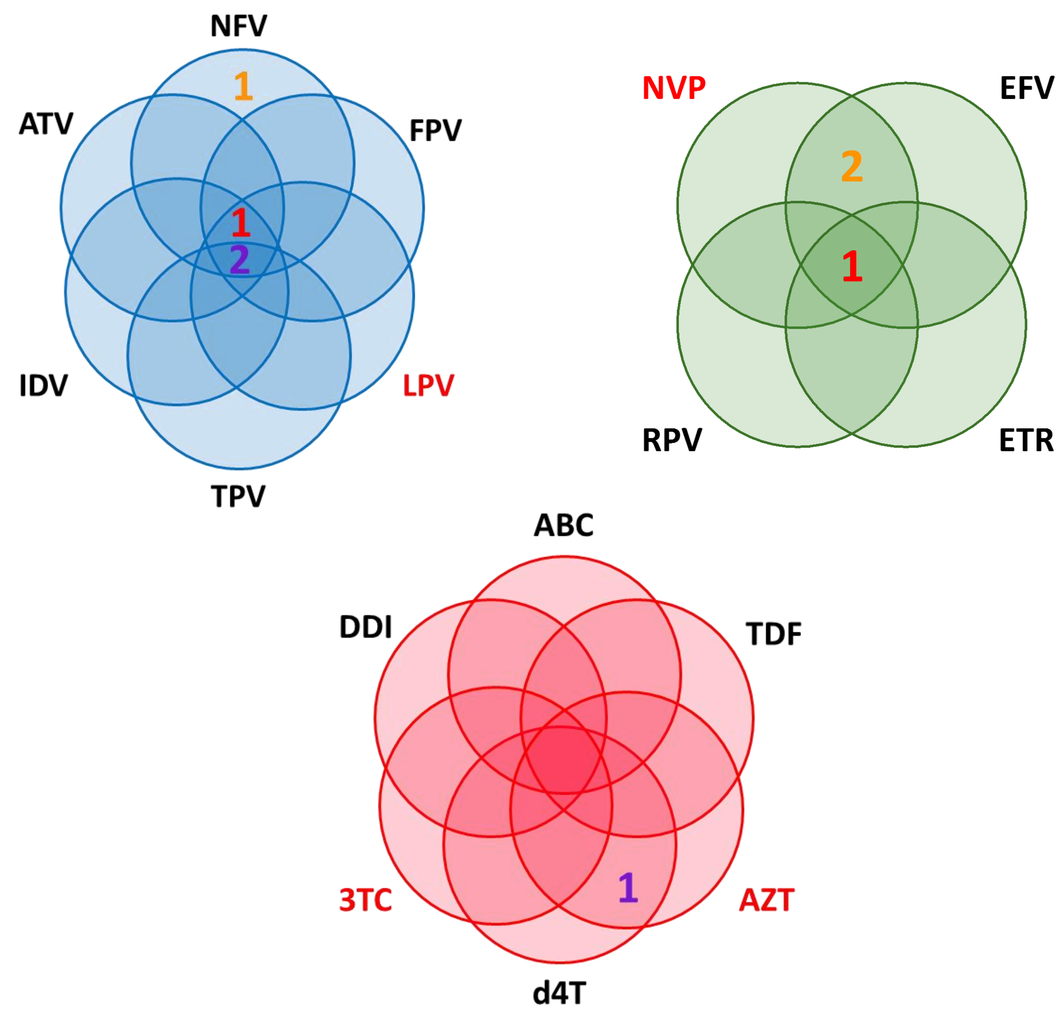

Figure 3. Drug resistance mutations influence in the available antiretroviral drugs of each class. Each circle represents one ARV drug, and those that compose the first line therapy recommendations are colored red.

Conclusions

- These results indicate an increase in the HIV-1 diversity and a probable change in the TDRM profile in Rio de Janeiro between the two periods.
- The prevalence of HIV-1 TDRM in this population could affect the virological outcome of the standard first-line ARV regimens to prevent HIV vertical transmission, reinforcing the importance of continuous monitoring of the HIV-1 genetic diversity and TDRM in Brazil.

Financial support: FAPERJ Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro; IOC Instituto Oswaldo Cruz