Acquired HIV-1 Drug Resistance in perinatal HIV

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BACKGROUND

- Children and adolescents with perinatal HIV have a high risk of development of drug resistance mutations (DRM).
- Acquisition of DRM is related to non-adherence and frequent treatment switches in this vulnerable population.
- Aim: assess the cumulative prevalence of major DRM in adults with perinatal HIV compared to matched individuals with horizontally acquired HIV and evaluate possible associated factors.

METHODS

- Case-control study comparing all MoCHiV and SHCS participants with perinatal HIV after transfer to adult care (**cases**) to matched SHCS participants with horizontally acquired HIV (**controls**).
- Inclusion criteria: antiretroviral treatment (ART) and ≥1 available genotypic resistance test.
- Matching was based on sex, year of diagnosis and time since ART initiation and the matching ratio was 1 case for 3 controls.
- Descriptive statistics was used to summarize patients characteristics and DRM prevalence, negative-binomial regression for risk factor analysis with number of cumulative DRM and acquired DRM as outcome variable.

RESULTS

Descriptive analysis:

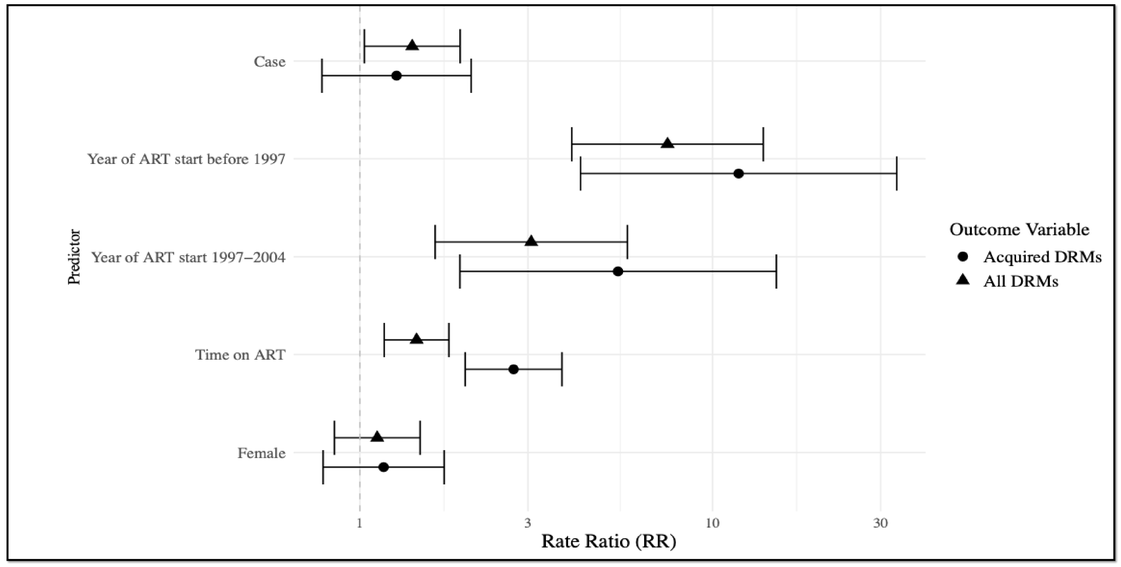
- 83 cases and 253 controls were included in the analysis.
- Major DRM to ≥1 ART class were present in 51 (63%) cases and in 156 (61.7%) controls, with nucleoside reverse transcriptase inhibitor (NRTI) being the most affected class in both groups (58% vs 54.5%). (**Table 1**)
- Resistance to integrase strand transfer inhibitor (INSTI) was rare (1.2% vs 2.8%). (**Table 2**)

TABLE 3: RATE RATIOS FOR HIV DRM OUTCOMES

Model	Term	RR (CI)
Acquired DRMs	Case	1.27 (0.78, 2.07)
Acquired DRMs	Time on ART	2.73 (1.99, 3.74)
Acquired DRMs	Female	1.17 (0.79, 1.73)
Acquired DRMs	Year of ART start before 1997	11.87 (4.23, 33.32)
Acquired DRMs	Year of ART start 1997-2004	5.4 (1.92, 15.17)
All DRMs	Case	1.41 (1.03, 1.92)
All DRMs	Time on ART	1.45 (1.17, 1.79)
All DRMs	Female	1.12 (0.85, 1.48)
All DRMs	Year of ART start before 1997	7.46 (3.99, 13.94)
All DRMs	Year of ART start 1997-2004	3.06 (1.63, 5.74)

Cumulative prevalence of major DRM was high both in individuals with perinatal HIV and with horizontally acquired HIV.
The risk of DRM was driven by ART duration and exposure to earlier, low-barrier regimens rather than by perinatal HIV acquisition *per se*.

FIGURE 1: RATE RATIOS FOR HIV DRM OUTCOMES



Note 1: The "Time on ART" variable was calculated as time from ART start to last available sequence for the "all DRMs model". For the "acquired DRMs" model it was calculated as time from first to last available sequences
Note 2: Acquired DRMs were defined as DRMs detected in subsequent genotype resistance testing but not at baseline
Note 2: Models accounted for matching; SD for random effect of matching for the models was as follows: Model with acquired DRMs: 0.0566, Model with all DRMs: 4.81 × 10−9
Note 3: Time on ART: rate ratio per 10 years
Note 4: The comparison group for "Year of ART start before 1997 and 1997-2004" is ART start after 2004

Risk factors analysis:

- No statistically significant difference in the risk of DRM was found between cases and controls.
- Overall, time since ART initiation and ART start before 2005 were the only significant risk factors associated with the occurrence of DRM. (**Figure 1 and Table 3**)

TABLE 1: PATIENTS CHARACTERISTICS

Table 1: Patients characteristics

Variable and unit	Cases	Controls	Overall
Sample size	81	253	334
Time on ART in years, median [IQR] [1]	15.36 [9.25, 19.99]	14.92 [8.76, 18.73]	15.04 [9.00, 19.21]
Age at ART start in years, median [IQR]	7.37 [2.78, 12.42]	34.34 [29.46, 41.10]	28.20 [9.83, 36.22]
Age at diagnosis, median [IQR]	3.09 [0.07, 7.55]	31.54 [27.81, 39.81]	25.21 [4.76, 34.41]
Male sex, n (%)	35 (43.2)	107 (42.3)	142 (42.5)
Ethnicity, n (%)			
White	48 (59.3)	173 (68.4)	221 (66.2)
Black	27 (33.3)	60 (23.7)	87 (26.0)
Asian	3 (3.7)	5 (2.0)	8 (2.4)
Hispano-American	1 (1.2)	9 (3.6)	10 (3.0)
Other/Unknown	2 (2.5)	6 (2.4)	8 (2.4)
Education, n (%)			
Higher education	10 (12.3)	54 (21.3)	64 (19.2)
Mandatory school [2]/Finished apprenticeship	66 (81.5)	156 (61.7)	222 (66.5)
No completed school or professional education	3 (3.7)	27 (10.7)	30 (9.0)
Other/Unknown	2 (2.5)	16 (6.3)	18 (5.4)
Adherence, n (%) [3]			
Adherent	46 (56.8)	175 (69.2)	221 (66.2)
Not adherent	24 (29.6)	69 (27.3)	93 (27.8)
Unknown	11 (13.6)	9 (3.6)	20 (6.0)
CD4 nadir in cells/ul, median [IQR]	227.00 [78.25, 470.00]	146.50 [49.00, 243.00]	159.50 [56.00, 267.25]
Mean log RNA, median [IQR]	4.77 [3.06, 6.47]	4.58 [2.98, 6.24]	4.63 [2.98, 6.25]
Treatment switches, median [IQR]	9.00 [4.00, 17.00]	8.00 [4.00, 14.00]	8.00 [4.00, 14.75]
ART, n (%)			
PI [4]	69 (85.2)	204 (80.6)	273 (81.7)
NNRTI [5]	54 (66.7)	164 (64.8)	218 (65.3)
INSTI [6]	34 (42.0)	81 (32.0)	115 (34.4)

[1] Time in years from antiretroviral treatment start to the last performed resistance test
[2] Mandatory school: 9 years in Switzerland
[3] Adherence was assessed at every follow up according to the frequency of missed doses. A numeric score ranging from 0 (i.e. never missed a dose) to 5 (i.e. missed a dose every day) was used. Patients were defined as adherent over the entire study period if they reported a score of either 0 or 1 in most (i.e. > 50%) of the assessments
[4] Number of patients that have ever received a PI-based treatment
[5] Number of patients that have ever received a NNRTI-based treatment
[6] Number of patients that have ever received a INSTI-based treatment

TABLE 2: PREVALENCE OF MAJOR DRM

Table 2: Overview of major DRM

Number of patients	Cases	Controls	Overall
Sample size	81	253	334
DRM to ≥ 1 drug class, n (%)	51 (63.0)	156 (61.7)	207 (62.0)
PI	18 (22.2)	38 (15.0)	56 (16.8)
NNRTI	30 (37.0)	81 (32.0)	111 (33.2)
NRTI	47 (58.0)	138 (54.5)	185 (55.4)
INSTI	1 (1.2)	7 (2.8)	8 (2.4)
DRM to 1 drug class, n (%)	18 (22.2)	73 (28.9)	91 (27.2)
DRM to 2 drug classes, n (%)	22 (27.2)	62 (24.5)	84 (25.1)
DRM to ≥ 3 drug classes, n (%)	11 (13.6)	21 (8.3)	32 (9.6)
DRM at first sequencing, n (%)	40 (49.4)	88 (34.8)	128 (38.3)
Delta DRM (%) [1]	31 (38.3)	109 (43.1)	140 (41.9)

[1] Count of acquired DRM in the timespan from the first to the last sequencing.