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Letter to the Editor

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Pregnancies in perinatally HIV-infected women: antiretroviral treatment strategies, obstetric and virologic outcomes

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Sir,

Management of pregnancy in perinatally HIV-Infected adolescents and young women constitutes a challenge for clinicians. Prior reports described high rates of advanced disease, irregular adherence to antiretroviral therapy (ART) and suboptimal virologic suppression at delivery [1-6]. Data about maternal and neonatal outcomes in first and subsequent pregnancies in this population remains understudied and may provide useful information in order to optimize clinical approach.

We performed a retrospective chart review of pregnancy-events assisted by a multidisciplinary working group [7] in a tertiary hospital in Buenos Aires, Argentina between 2008-2016. For those patients with >1 pregnancy, certain variables were compared between first and ulterior pregnancies. "Non-standard ART" was defined as prescription of, at least, one non-preferred drug for pregnancy (according to corresponding national guidelines at the year of follow-up), any regimen containing more than 3 drugs, or any nucleos(t)ide (NRTI)-sparing treatment. Data were processed with *Statistix* 7.0 software (chi-square and fisher exact test).

Fifty pregnancies in 34 women were followed, corresponding to 33 first and 17 ulterior pregnancies (15 patients had 2 pregnancies; 5 had 3 or more). Globally, the median (interquartile range) of age, gestational age, viral load (VL) and CD4 T-cell count were: 19 years (17-22); 12 weeks (8-23); 1333 copies/mL (<34-13777) and 283/µL (150-512). Sixty-eight percent had a previous AIDS-defining diagnoses. Despite all had a prescription of ART prior to pregnancy, 33% had detectable viremia at first visit. This population was heavily pretreated with a median of 3 (1-4) prior regimens. Resistance mutations (RAMs) were observed in 88% of patients and 80% harbored multi-class resistant HIV. Predominant mutations were: 1) for NRTIs: timidine analogue-RAMs (47.6%) and M184V (38%); 2) for non-nucleoside reverse transcriptase inhibitors: K103N/S (42.8%), Y181C (14.2%), G190S/A (14.2%) K101P/Q/E (14.2%); 3) for protease inhibitors: L90M (33.3%), I54V (28.5%), V82A (23.8%), M46I (19%). Nonstandard ART was required in 34%, being as follows: 1) boosted-protease inhibitor + 2 NRTIs + another drug as raltegravir, T-20 or maraviroc (18%); 2) Non-standard NRTIs (d4T or ddI or combined ABC and TDF) containing ART (8%); 3) ART with three NRTIs (3TC + AZT + TDF, 6%); 4) NRTI-sparing ART (one patient with DRV/r, RAL and EFV, 2%). Noncompliance to ART was observed in 38% of patients. Due to detectable viremia close to delivery, prescription of an additional drug as intensification strategy was required in 12 (26%: 9 addition of raltegravir; 2 enfuvirtide; 1 dolutegravir).

Considering virologic outcomes, 77% achieved VL </=50 at delivery. One patient died due to an opportunistic disease (*Pneumocystis* pneumonia). Obstetric complications occurred in 25% (being the most frequent threatened preterm labor and hemorrhage); 12% had a spontaneous abortion; 2% intrauterine fetal death. Most frequent mode of delivery was elective cesarean section (56.4%) while 11% of births were preterm. Neonatal outcomes were as follows: 20% had low-birth weight, 6% congenital malformations and mortality was 2%. Use of combination neonatal prophylaxis (either AZT + 3TC or AZT + 3TC + NVP) was required in 16% of newborns. After delivery, 4 mother-child binomium were lost to follow up (9.2%) before baseline neonatal virologic evaluation. No vertical transmission was documented to date among those who remained under follow up: 44.7% of newborns had negative HIV-1 antibody tests at 18 months of life, 42% had at least 2 negative PCRs after 2 months and the rest had 1 negative PCR at 2 months. Description of variables in first and ulterior pregnancies is shown in table 1 (*p* value non-significant for all comparisons).

As far as we know, this is the biggest cohort of perinatally HIV-infected pregnant women in Latin America. Several

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Table 1 **Comparison of first vs. subsequent pregnancies (selected variables) in perinatally HIV-infected adolescents and young women.**

Variable	First pregnancy (N = 34)	Ulterior pregnancy (N = 17)
Gestational age at first visit (median, IQR)	10 (8-23)	15 (9-23)
Detectable baseline viral load[a] n, (%)	10 (30,3)	5 (38,5)
Late ART initiation[b] n, (%)	7 (21,9)	4 (25,1)
Irregular adherence to ART n, (%)	11 (35,5)	6 (42,9)
Requirement of intensification strategies in third trimester[c] n, (%)	4 (23,5)	9 (27,3)
Detectable viral load at delivery[a] n, (%)	6 (24)	4 (28,4)

ART: antiretroviral therapy; IQR: interquartile range

[a]Viral load >50 copies/mL; [b]after first trimester; [c]addition of another antiretroviral drug due to insufficient virologic response

aspects of this population should be highlighted. Prevalence of RAMs was extremely high and precluded the prescription of standard ART in a considerable proportion of patients. Considering this information, access to novel drugs should be warranted in order to provide ART with, at least, 2 or 3 fully active drugs. Adding complexity, an overall high rate of nonadherence to ART was observed, which should be attributable, mostly, to psychosocial issues. This is consistent with other reports [1-6]. Of note, no improvement was observed in subsequent gestations what suggests that adherence issues exceed pregnancy period, remaining a challenge for virological success. In this context, a high percentage of patients, in any pregnancy, required intensification strategies (mostly with integrase inhibitors) in order to obtain a rapid viral load reduction close to delivery [8]. An overall high rate of obstetric complications, with predominance of abortion was described, what indicates the requirement of strict obstetric follow-up. Despite this complex scenario, no cases of perinatal transmission occurred, what highlights the need of opportune interventions and interdisciplinary approach. Prospective cohorts in our region are needed in order to better define ART strategies and clinical approach for this population.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest

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