# Resistance in Young Children Newly Diagnosed with HIV in Western Cape, South Africa

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## BACKGROUND

- Pretreatment drug resistance among children living with HIV (CLHIV) can potentially compromise antiretroviral therapy (ART) effectiveness
- Drug resistant HIV may be directly transmitted during vertical acquisition or resistance may be acquired in infants with HIV following exposure to antiretrovirals consumed through breastfeeding or administered as prophylaxis

## METHODS

- We performed resistance testing in young CLHIV (age <3 years) newly diagnosed with HIV in Western Cape, South Africa (July 2021 to October 2022) who either (1) acquired HIV via possible breastfeeding transmission from mothers who received ART (any regimen) during pregnancy/postpartum and/or (2) were exposed to protease inhibitors (PIs) or integrase strand transfer inhibitors (INSTIs) in utero
- Possible breastfeeding transmission was defined as a positive HIV-PCR test at age >28 days, which occurred after a previous negative HIV-PCR test
- We limited mutations included to those recommended for surveillance of transmitted drug resistance

Table: Mutations detected in children at the time of HIV diagnosis (frequencies in parentheses)

| |
|---|
| **NNRTI-associated mutations (n=135 NNRTI sequences)** |
| K101E (6), K103N (54), K103S (3), V106A (1), V106M (8), Y181C (2), Y188H (1), Y188L (3), G190A (8), G190E (1), P225H (14) |
| **NRTI-associated mutations (n=135 NRTI sequences)** |
| D67N (2), T69D (1), K70E (2), M184V (7), L210W (1), T215D (1), K219Q (2) |
| **PI-associated mutations (n=135 protease sequences)** |
| L90M (1) |
| **INSTI-associated mutations (n=122 INSTI sequences)** |
| T97A (1), G118R (1), E138K (1) |

Abbreviations: NNRTI non-nucleoside reverse transcriptase inhibitor, NRTI nucleoside reverse transcriptase inhibitor, PI protease inhibitor, INSTI integrase strand transfer inhibitor

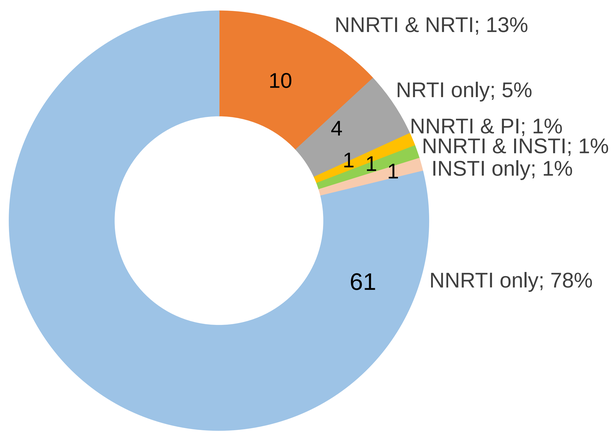
58% of children (n=78/135) had resistance mutations detected prior to ART start

Of these children, 94% had NNRTI-, 18% NRTI-, 3% INSTI-, and 1% PI-associated mutations

## RESULTS

- We included 135 newly diagnosed CLHIV for resistance testing, of whom 91% (n=123) had possible breastfeeding transmission
- Most mothers started ART before pregnancy (77%) and 46% were exposed to ≥3 classes of ART prior to infant diagnosis
- ART regimens that mothers were most commonly exposed to before delivery were NNRTI-based (n=102/129; 79%), largely efavirenz-based
- After delivery (prior to infant diagnosis), exposure to dolutegravir-based regimens was more common (n=57/99; 58%)
- Overall, 58% of CLHIV (n=78/135) had resistance mutations detected and 15% of those with mutations (n=12/78) had mutations to more than one class
- NNRTI-associated mutations were common (n=73/78; 94%)
- NRTI-, INSTI- and PI-associated mutations were found in 18% (n=14/78), 3% n=(2/78) and 1% (n=1/78) of CLHIV with mutations, respectively
- One child with breastfeeding transmission of HIV, had high-level INSTI and NNRTI resistance detected at age 18 months at HIV diagnosis (E138K, G118R and K103N mutations). The child previously tested HIV-PCR negative at birth, 10 weeks, and 6 months. The mother had elevated viral load (VL>1000 copies/ml) during pregnancy and postpartum, and changed from efavirenz- to dolutegravir-based ART 13 months after delivery. She was virally suppressed (VL<50 copies/ml) at the time of infant diagnosis. The findings suggest possible acquisition of dolutegravir resistance due to exposure to dolutegravir in breastmilk, or resistance may have been transmitted

Figure: Drug class/es of mutations detected in 78 infants




## CONCLUSIONS

- NNRTI-associated mutations are common and may be transmitted or arise from exposure to NNRTIs as prophylaxis or in breastmilk
- Dolutegravir is the preferred first-line treatment for both adults and CLHIV older than 4 weeks and very low INSTI resistance levels have been observed in adults, but limited data exist on genotyping the integrase region in CLHIV
- The prevalence of pretreatment INSTI resistance in CLHIV is likely to be very small but future surveillance, including longitudinal studies with paired mother-infant resistance testing, is needed

## ADDITIONAL INFORMATION

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