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HIV Drug Resistance Patterns Among Pregnant Women After Dolutegravir Scale-Up in Sub-Saharan Africa

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BACKGROUND

- In Sub-Saharan Africa (SSA), HIV drug resistance (HIVDR) rates for non-nucleoside reverse transcriptase inhibitors (NNRTI) are high in patients with antiretroviral treatment failure, with implications for the risk of HIV mother-to-child transmission among pregnant women.
- Since 2019, the WHO recommends an integrase strand transfer inhibitor (INSTI) - dolutegravir (DTG) - for first-line antiretroviral treatment (ART) regimens.
- We aimed to describe HIVDR mutations among pregnant women living in SSA at the time of DTG scale-up.

METHODS

Study design: Observational study nested in a malaria prevention clinical trial conducted in Gabon and Mozambique (2019-2023).

Population: Samples collected from 99 pregnant women living with HIV with virological failure (HIV viral load >400 copies/mL) at the first antenatal care (ANC) visit.

Analysis: Analysis of serum samples using Illumina MiSeq®.

Drug susceptibility was predicted using the Stanford HIVdb scoring system.

Table 1. Characteristics at the first ANC visit according to the presence of HIVDR mutations.

Characteristics	At least one HIVDRM	No HIVDRM
	n (%) or median [IQR]	
Age (years)	29 [23-34]	24 [22-27]
Country		
Gabon	6 (37.5)	10 (62.5)
Mozambique	33 (39.8)	50 (60.2)
Previous pregnancies		
0-3	25 (64.1)	57 (95.0)
4 or more	14 (35.9)	3 (5.0)
Haemoglobin (g/dL)	10.3 [9.2-11.0]	10.8 [9.6-12.5]
Viral load (copies/mL)	12895 [3556-32700]	19510 [4699-49403]
On ART at baseline	25 (64.1)	13 (21.67)
TDF + 3TC + EFV	9 (23.1)	1 (1.7)
TDF + 3TC + DTG	15 (38.5)	12 (20.0)
TDF + 3TC + LPV/r	1 (2.56)	0 (0)

- The prevalence of HIVDR mutations for NNRTIs in pregnant women from Gabon and Mozambique was above 10% (WHO recommended threshold of pre-treatment drug resistance for changing ART regimen).
- HIVDR mutations for INSTIs remained low with 6.1%.
- In two participants with virological failure from Mozambique, major resistance mutations for INSTIs were identified, calling for continued surveillance of HIV drug resistance.

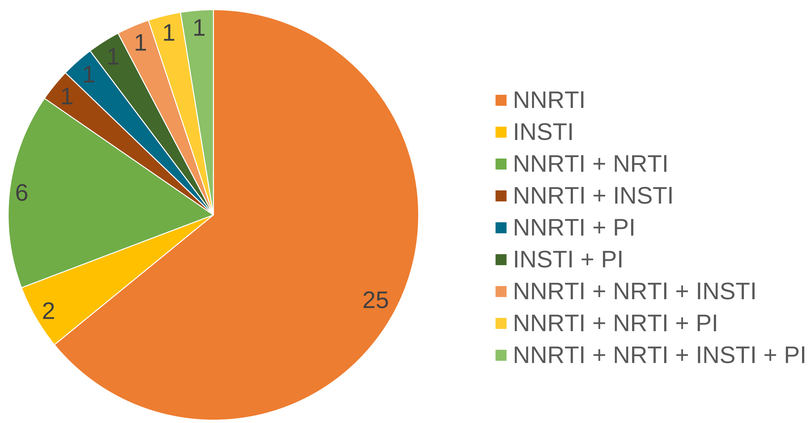


Figure 1. Frequency of resistance mutations by drug category at the first ANC visit among participants with HIVDR mutations.

NNRTI - Non-nucleoside reverse transcriptase inhibitors, INSTI - Integrase strand transfer inhibitor, PI - Protease inhibitor, NRTI - Nucleoside reverse transcriptase inhibitor.

RESULTS

- Out of 99 women, 39 had at least one HIVDR mutation at their first ANC visit.
- Median age was higher in women with HIVDR mutations compared to those without (29 vs 24 years; p=0.009).
- A higher proportion of women were on ART in the group with HIVDR mutations compared to the group without (64.1% vs 21.7%; p<0.001)
- NNRTI mutations were detected in 36 (36.4%) women and INSTI mutations in 6 (6.1%) women.
- Two major mutations for INSTIs were detected:
  - G118R (5-10 fold reduced susceptibility to DTG) in a participant receiving DTG based regimen (DTG resistance mutation score: 60).
  - R263K (2 fold reduced susceptibility to DTG) in a participant receiving EFV based regimen (DTG resistance mutation score: 30).

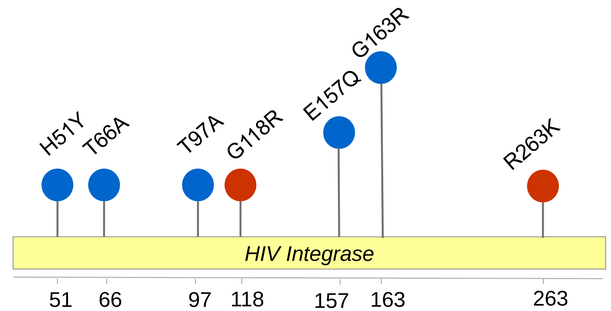


Figure 2. INSTI resistance mutations among participants at enrolment.

*G118R and R263K major INSTI resistance mutations conferring reduced susceptibility.

CONCLUSIONS

- The prevalence of INSTI mutations was low in the early phases of DTG scale-up
- The finding of a mutation against DTG in an INSTI-naïve pregnant woman from Mozambique calls for continued surveillance of HIV drug resistance in vulnerable and high-risk populations from SSA.

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