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EASTERN CAPE
HEALTH

HVDRS STUDY

HIV-1 DRUG RESISTANCE SURVEILLANCE AMONG PARTURIENT WOMEN ON ANTI-RETROVIRAL THERAPY IN THE EASTERN CAPE, SOUTH AFRICA

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HIV DRUG RESISTANCE SURVEILLANCE (HVDRS) STUDY GROUP

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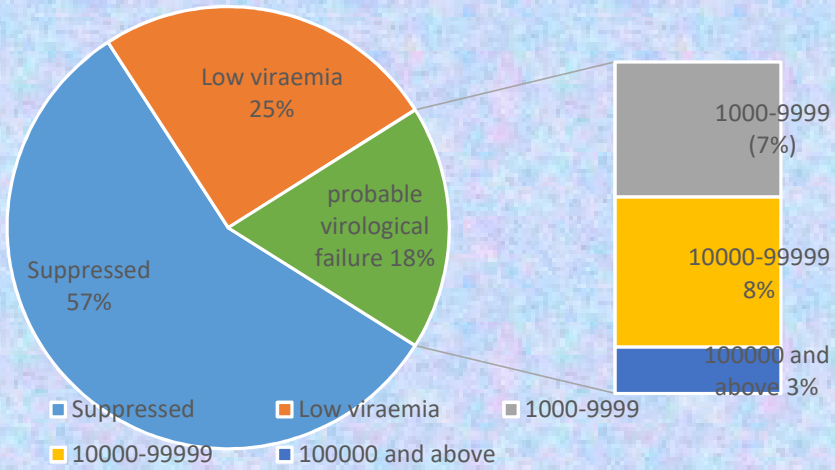
BACKGROUND

- HIV prevalence of 30.8% among pregnant women and over 95% ART coverage in the country(1,2).
- About 320, 000 children were living with HIV in SA and 12,000 new paediatric infections occurred in 2016(3).
- Emergence of HIV drug resistance is inevitable and poses significant threat to achieving the goal of elimination of mother-to-child transmission (4,5,6).

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RESEARCH ARTICLE Open Access

Factors affecting adherence to antiretroviral therapy among pregnant women in the Eastern Cape, South Africa

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Abstract

Background: Context-specific factors influence adherence to antiretroviral therapy (ART) among pregnant women living with HIV. Gaps exist in the understanding of the reasons for the variable outcomes of the prevention of mother-to-child transmission (PMTCT) programme at the health facility level in South Africa. This study examined adherence levels and reasons for non-adherence during pregnancy in a cohort of parturient women enrolled in the PMTCT programme in the Eastern Cape, South Africa.

Objectives

- **To assess the burden of "Drug Resistance Mutations" (DRMs) in a cohort of parturient women who delivered their index babies at high viral load.**

- **To examine the patterns and determinants of DRMs in a failing cART regimen from pregnant women in the cohort.**

Findings on the frequency and pattern of HIV drug resistance mutations in pregnant women with high VL might inform new strategies and innovations in the efforts towards eliminating MTCT.

.....Methodology

- Design: Laboratory based study
- Settings: Venous blood of pregnant women with high viral load on ART at delivery were sampled at Frere and Cecilia Makiwane Hospital, Eastern Cape.
- Ethical approval was granted by WSU & ECDoH.
- CEOs gave permission. Written informed consent by participants.

- We conducted analysis of the Pol sub-genomic sequence of RNA derived from plasma samples of 80 women with probable virological failure at delivery between January and May 2018.
- Partial pol gene covering 1030bp were amplified and sequenced according to standard protocols.
- DRMs were determined by submitting the generated partial pol sequences to the Stanford Genotypic Resistance interpretation algorithm (http://hivdb.stanford.edu/pages/algs/HIVdb.html) for query on mutations associated with drug resistance.
- We also examined the correlates of DRMs using bivariate analysis.

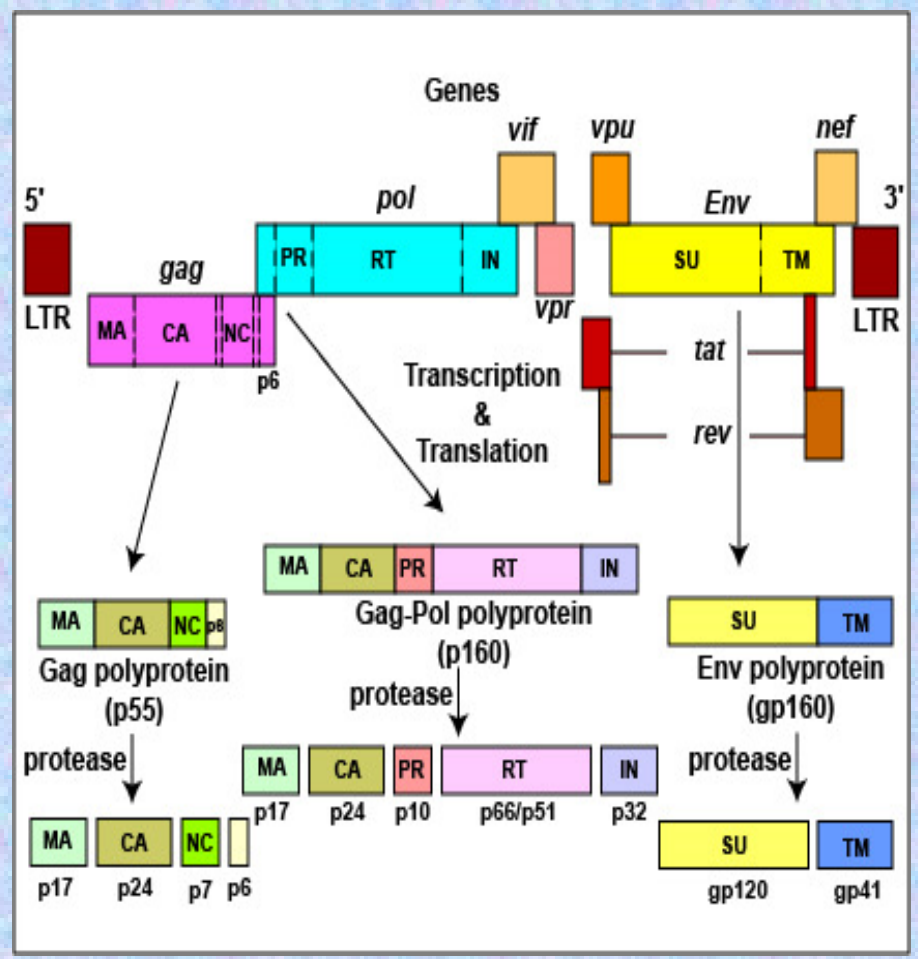

Fig. 1. Schematic representation of HIV-1 genome. All the important open reading frames are shown

RESULTS

Characteristics of the participants

- Ages ranged from 16 - 43 years; mean of 30.2 (±6.2) years

- Predominantly:
  - Single (86.3%)
  - WHO Clinical Stage 1 (62.0%),
  - Efavirenz-based regimen (82.5%, n=66)
  - Minimum duration on ART of 12 months (65%)

- Median durations:
  - First line = 21 months
  - Second line = 42 months
  - After switching ART regimen = 11 months

- Mean **CD4 count = 273 [**interquartile range (IR): 3 – 759]

- Mean viral load = **5.1 logs** (IR: 3.0 – 6.5 logs)

Drug Resistance Mutations (DRMs) in Viral Sequences

- DRMs occurred in 58 viral sequences (72.5%)
  - **Efavirenz-based cART = 69.7% ()**
  - **Protease inhibitor-based cART = 87.7% ()**

- Predominant mutation was K103N (n=43; **74.1%**)
  - **Efavirenz-based cART = 79.1% (n=34)**
  - **Protease inhibitor-based cART = 20.9% (n=9)**
  - **Durations on Protease inhibitor-based cART: 4 months (n=5), 15, 17, 40 and 52 months.**

Drug Resistance Mutations in Viral Sequences

Drug Resistance Mutations	Frequency	Percentages (%)
Major NNRTI Mutations		
*K103N	43	74.1
V106M	9	15.5
V108I	5	8.6
P225H	10	17.2
K101E	2	3.4
Y188L	4	6.9
Major NRTI Mutations		
*M184V	28	48.3
*K65R	11	19.0
K70R/E (TAM)	4	6.9
K219Q (TAM)	4	6.9
Major PI Mutations		
V82L	1	1.7
L90M	1	1.7

Bivariate Analysis of Clinical Correlates of HIV Drug Resistance

Variables	All	Resistance	No resistance	p-value
CD4 Count				
<200	23 (34.3)	23 (95.7)	1 (4.3)	0.002
200-349	24 (35.8)	13 (54.2)	11 (45.8)	
350-499	14 (20.9)	11 (78.6)	3 (21.4)	
≥500	6 (9.0)	2 (33.3)	4 (66.7)	
WHO Stage				
I	44 (62.0)	28 (63.6)	16 (36.4)	0.304
II	11 (15.5)	9 (81.8)	2 (18.2)	
III	14 (19.7)	12 (85.7)	2 (14.3)	
IV	2 (2.8)	1 (50.0)	1 (50.0)	

DISCUSSION
&
CONCLUSIONS

- With accelerated scale-up of ART, the emergence of HIV drug resistance mutations (DRMs) becomes inevitable in pregnant women (4,5,6).

- High prevalence of DRMs of 72.5% in women who delivered their index pregnancy at high viral load in the study settings.

- Emergence of acquired resistance is a direct consequence of suboptimal adherence reported by over 90% of the cohort.

- Persistence of K103N mutations for variable periods after switching regimen; role of ?**archived resistance or slow reversion of mutations in sub-optimal adherence**

K103N mutations has serious consequences for

infant prophylaxis and treatment

- Studies have demonstrated onward transmission of these maternal DRMs to newborns (7, 8).

- Clinicians should **monitor viral load and switch regimen** promptly while addressing ongoing adherence challenges to the new regimen.

- In conclusion, parturient women delivering at high viral load are at increased risk of acquiring DRMs, which could compromise the infant prophylaxis and increase MTCT risks.

- A point-of-care reverse transcriptase-PCR for screening for common resistance mutations will guide appropriate neonatal prophylaxis and maternal therapy.

Adeniyi OV, Obi CL, Ter Goon D, Iweriebor B, Ajayi AI, Lambert J, Okoh A. HIV-1 Drug Resistance Surveillance among Parturient Women on Anti-retroviral Therapy in the Eastern Cape, South Africa: Implications for Elimination of Mother-To-Child Transmission. Journal of Clinical Virology. 2019; 117: 89 – 95.

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