00719

Severe Immune Suppression and Retention Among Infants in South Africa

Gabriela E Patten[1], Nosisa Sipambo[2], Karl-Günter Technau[3], Jonathan Euvrard[1], Nathan Ford[1], Mary-Ann Davies[1]

[1]Centre for Infectious Disease Epidemiology and Research, University of Cape Town, Cape Town, South Africa, [2]Harriet Shezi Children's Clinic, Chris Hani Baragwanath Academic Hospital, Department of Paediatrics & Child Health, University of Witwatersrand, Johannesburg, South Africa, [3]Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

BACKGROUND

- After rapid improvements in HIV programmes, children are now starting antiretroviral therapy (ART) younger and in a healthier state.
- Among infants sustained retention and adherence to ART is especially challenging, and it is possible that severe immune suppression (SIS) will be increasingly seen among those on ART.
- We aimed to describe SIS at ART start and on ART, and retention among infants on ART in South Africa.

METHODS

- Using data from 3 International epidemiology Databases to Evaluate AIDS (IeDEA) Southern Africa cohorts, we describe SIS at ART start and on ART between 2007-2020.
- We included infants aged <1 year with a CD4 cell count / % measured at ART start and ≥1 subsequent measure, and at least 9 months of follow-up between ART start and database closure (Oct 2018 – Mar 2021).
- SIS was defined according to WHO definition using age-based thresholds and CD4% or CD4 cell count where CD4% is not available.
- Lapse in care was defined as >9 months without a recorded visit.
- A multistate model was used to estimate transition probabilities between 5 states based on CD4 count/% after ART start: SIS on ART; Stable, not SIS; Early Lapse, lapse occurring <9 months from ART start; Late Lapse, lapse occurring ≥9 months on ART; and Death. (Fig 1)

Table 1: Characteristics and outcomes among infants initiated on ART in South Africa

	Year of ART Start			Total
	2007-2009	2010-2012	2013-2020	
Total	473	367	366	1206
Female	252 (53.3%)	205 (55.9%)	187 (51.1%)	644 (53.4%)
Median Age at ART start (years) (IQR)	0.48 (0.3-0.7)	0.36 (0.3-0.6)	0.27 (0.1-0.5)	0.37 (0.2-0.6)
Severely Immune Suppressed at ART star	**388 (82.0%)**	**269 (73.3%)**	**242 (66.1%)**	**899 (74.5%)**
Ever experienced viraemia*	274 (57.9%)	216 (58.9%)	224 (61.2%)	714 (59.2%)
Ever experienced SIS on ART	228 (48.2%)	147 (40.1%)	145 (39.6%)	520 (43.1%)
Death	10 (2.1%)	7 (1.9%)	7 (1.9%)	24 (2.0%)

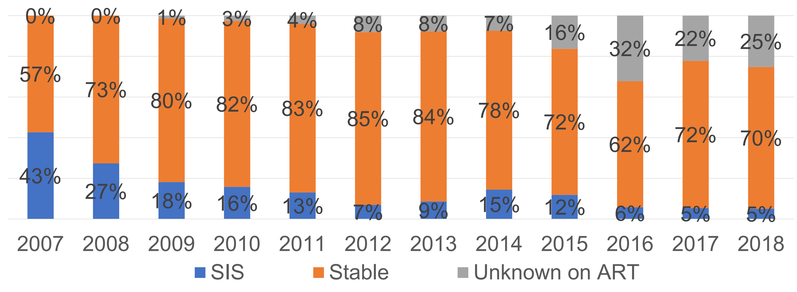
*Viral load ≥1000 copies/ml

Severe immune suppression (SIS) at ART start remains extremely high. Re-engaging in care with SIS is more likely among those starting ART more recently.

RESULTS

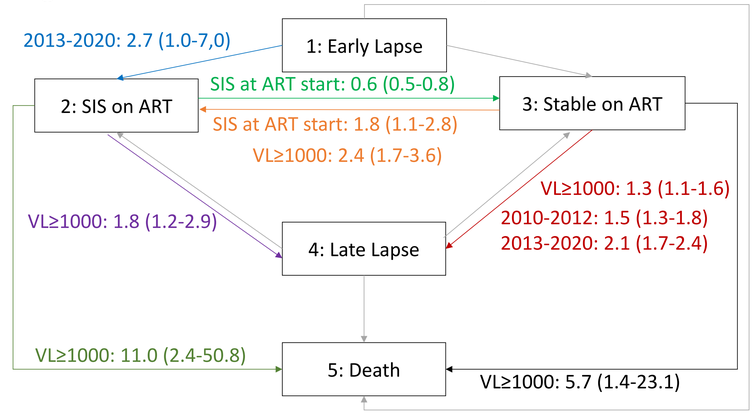
- In more recent years fewer infants initiated ART. SIS at ART start declined but remained very high. The proportion who experienced SIS on ART during follow-up initially declined with later year of ART start but plateaued after 2010. The proportion who experienced viraemia increased. (Table 1)
- Among those in care, the proportion of person-time spent SIS on ART initially declined but increased to 15% in 2014. (Fig 1) Subsequently time in care with unknown immune status (with no CD4 measure for >1 year) increased, with declining time spent in Stable or SIS on ART, indicating that lack of CD4 monitoring is potentially under-detecting SIS on ART.

Figure 1: Proportion of on ART person-time spent in each state



This publication was made possible by Grant Number UO1AI069924 from the NIH (NIAID, NICHD, NCI, NIDA, NIMH) (PI: Egger and Davies). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Figure 2: Multi-state model states and adjusted hazard ratios*



*Adjusted for year of ART Start (vs 2007-2009), sex (female vs male), SIS at ART start (vs not SIS at ART start), VL (VL≥1000 or VL missing, vs VL<1000 copies/ml)
Only significant associations shown

- Our multi-state model (Fig 2) found:
  - Those starting ART in the most recent years were more likely to transition from Early lapse to SIS on ART, later year was associated with increasing transition from Stable to Late Lapse.
  - Those with SIS at ART start were more likely to transition from Stable to SIS on ART, and less likely to transition to Stable from SIS on ART.
  - Those with viraemia were more likely to transition from Stable to SIS on ART, and more likely to transition from either of the on ART states (Stable or SIS) to Late Lapse and Death.

CONCLUSIONS

- Severe immune suppression at ART start among infants has declined but remains extremely high.
- Those starting ART most recently are particularly vulnerable to SIS on ART, being more likely to re-engage in care with SIS following an early lapse.
- Despite declining numbers, long-term retention is increasingly a challenge among those who become clinically stable.
- Viraemia strongly predicted death even from a clinically stable state, highlighting the difficulties of managing effective ART among infants.

Contact: gem.patten@uct.ac.za