Causes of death after early ART in infants living with HIV from 3 sub-Saharan African countries.

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BACKGROUND

Despite comprising only 4% of all positive people, children account for 15% of all HIV/AIDS-related deaths. Mortality unrelated to AIDS is also high in LMIC. We investigated causes of death, potential relationship with HIV infection, and associated factors in a cohort of early treated children.

METHODS

From May 2018 to May 2021, we recruited infants who initiated ART within the first 6 months of life and within 3 months of diagnosis. Follow-up was 4 years. There were 6 study sites in South Africa, Mozambique and Mali. HIV/AIDS related mortality was determined by an independent Endpoint Review Committee comprising three HIV Pediatric infectious disease specialists not directly involved in participant care. The experts assessed the relationship of each death to HIV advanced disease using available epidemiological, clinical, and laboratory data from the study database. Mortality risk factors were analyzed using a competing risk Cox multivariable regression model.

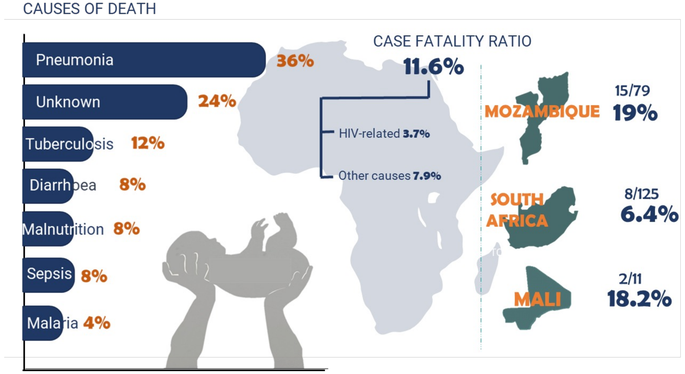


Fig 1. Causes of death and case fatality ratio.

Baseline viral load, CD4% slope and region are the main risk factors for early treated infants living with HIV (AIDS related or not)

RESULTS

Of 215 infants enrolled, the median age at HIV diagnosis was 31 days with ART initiation at a median age of 34 days [IQR 26.0;73.0]. Follow-up was 34.0 months [IQR 16.3;44.1]. Median VL at ART initiation was log 4.95 [IQR 3.58;5.82] copies/mL. Twenty-five infants (11.6%) died at a median age of 5.3 months [IQR 3.0;9.6]. The probability of death within the first year of ART initiation was 12% (95%CI 6-14), and after 2 and 3 years, 12% (95% CI, 8-17). The primary causes of death were pneumonia (36%), unknown (24%), tuberculosis (12%), malnutrition (8%), diarrhea (8%), sepsis (8%) and malaria (4%). Cause of death was assigned as likely HIV/AIDS-related in 8/25 (32%) of deaths. VL at ART initiation was significantly associated with all deaths (HIV/AIDS-related cause HR:3.0 (95%CI 1.3-7.1), p=0.014; unclear relation, HR:1.7 (95%CI 1.1-2.8), p=0.019). The more positive the CD4 slope, the lower the probability of death in HIV/AIDS-related (HR:0.7 (95%CI 0.5-1.0, p=0.067) or unrelated (HR:0.7 (95%CI 0.5-0.9), p=0.007). Patients from Mali had a higher probability of death from HIV/AIDS-unrelated causes , compared to those enrolled in South Africa (HR:13.8 [95%CI 1.92-98.8], p=0.009).

Table 1. Risk factors associated with mortality (HIV/AIDS-related and unclear relationships mortality).

	Relationship with HIV/AIDS	Hazard Ratios (95% CI)	p-value
Survival model			
Baseline viral load **(log10 copies/mL)**	HIV/AIDS-related Unclear relationship	2·98 (1·25-7·12) 1·75 (1·09-2·80)	**0·014** **0·019**
Sex (Ref. Female)	HIV/AIDS-related Unclear relationship	1·12 (0·21-6·01) 2·02 (0·73-5·55)	0·892 0·171
CD4% slope	HIV/AIDS-related Unclear relationship,	0·69 (0·46-1·03) 0·68 (0·51-0·90)	**0·067** **0·007**
Age at ART	HIV/AIDS-related Unclear relationship	1·38 (0·93-2·04) 0·86 (0·57-1·29)	0·110 0·461
Region (Ref: South Africa) **Mozambique** **Mali**	HIV/AIDS-related Unclear relationship HIV/AIDS-related, Unclear relationship	1·40 (0·28-7·07) 2·04 (0·74-5·67) 0·001 (0·00-0·001) 13·8 (1·92-98·8)	0·680 0·170 **<0·001** **0·009**

CONCLUSIONS

Mortality, both related with HIV/AIDS or probably unrelated, were associated with baseline VL and poor CD4 restoration. However, the 3-fold risk for high baseline VL and HIV/AIDS-related causes supports a strong biological effect of baseline VL along with a challenging social environment.

ADDITIONAL KEY INFORMATION

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