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Mortality Among Children Under Five Years of Age Living With HIV on Antiretroviral Treatment From HIV Case Surveillance Data, Malawi, 2022

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Abstract

From Malawi's HIV case surveillance, we report clinical characteristics and outcomes of 4461 children living with HIV on antiretroviral treatment aged <5 years from January to December, 2022. Among the 4% of children living with HIV who died, 43% were asymptomatic, 35% had advanced or severe symptoms at the time of HIV diagnosis and 50% died within 6 months of receiving an HIV diagnosis.

Keywords

HIV; mortality; Malawi; children; case surveillance

Accurate vital statistics among people with HIV are necessary to monitor trends and prevent HIV-related mortality. HIV case surveillance systematically and continuously collects available demographic and sentinel event data, such as clinical laboratory values and updates to an individual's clinical status, to characterize the HIV epidemic and guide program improvement.¹ In 2020, Malawi began a phased implementation to extract person-level clinical data from electronic health records for use in HIV case surveillance, which allows for analyses among persons diagnosed with HIV and enrolled in care.

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Children living with HIV (CLHIV), under the age of 5 years (<5), experience disproportionately poor outcomes, including mortality, compared with people living with HIV ≥5 years of age.² Recent published data have demonstrated that this disproportionately higher mortality in CLHIV <5 compared to people living with HIV ≥5 years of age occurs even among those on antiretroviral treatment (ART).³ However, little is known about the clinical characteristics of CLHIV <5 and the potential risk factors associated with their mortality. This analysis reviews clinical characteristics and outcomes among CLHIV <5 on ART using HIV case surveillance data in Malawi from January to December, 2022.

METHODS

HIV case surveillance consists of individual-level routinely collected data from point-of-care HIV services, beginning with HIV testing and counseling services, which were then sent to the national level for deduplication, reporting and routine analysis. HIV case surveillance data were pulled from Malawi's National Central Data Repository and included deidentified, individual-level data from 578 ART clinics in 27 districts. In 2022, the Central Data Repository included HIV case surveillance data for approximately 95% of all people living with HIV on ART in Malawi. Data were included in this analysis if the individual was less than 5 years of age and had a recorded clinic status reported from January to December, 2022. Clinic status included CLHIV who were on treatment (actively receiving ART), transferred out (transferred out of a clinic but have not yet been reported to have re-entered care), defaulted (missed their clinic appointments within the past 3 months), stopped treatment (missed clinic appointment more than 3 months ago) and deceased (CLHIV who were reported to have died as a sentinel event within the case surveillance system). Age was either the child's age on the last day of the year for those on treatment (December 31, 2022) or calculated based on the individual's age on the date they transferred out, defaulted, stopped treatment or died. Frequencies and proportions were calculated based on available clinical and demographic data, including clinic status, biological sex (female or male), age at the time of their clinic status (0–4 years), age at the time of HIV diagnosis (0–4 years), World Health Organization initial stage of symptoms at diagnosis (asymptomatic, mild, advanced and severe),⁴ time from HIV diagnosis to ART initiation (started same day, started within 2–13 days, delayed start ≥14 days) and time from HIV diagnosis to current clinic status (<6 months, 6 months to <1 year, 1 year to < 2 years, 2 years to <5 years). Data were excluded from our analysis if data appeared to contain errors, such as HIV diagnosis date prior to the date of birth or ART initiation date prior to HIV diagnosis, or if records did not otherwise meet the inclusion criteria. All variables were stratified by clinic status. Descriptive statistics, including frequencies and proportions, were calculated using STATA (version IC 16.1 Stat-aCorp, College Station, TX). This activity was reviewed by the CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy (eg, 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.). The Ministry of Health in Malawi has defined ethical standards and authorized the use of deidentified secondary analysis of case surveillance data as outlined in CDC cooperative agreements NU2GGH002301 and NU2GGH002427.

RESULTS

Among 47,886 total individuals on ART in Malawi's case surveillance system from January to December 2022, 4643 were children <5, of which 70 were excluded because the HIV diagnosis date preceded the date of birth and 112 were excluded because the ART initiation date preceded the HIV diagnosis date. Among the 4461 CLHIV <5 that were included in our analysis, the median age was 2 years (interquartile range: 1–3) and 51% were female. Most (70%, $n = 3102$) were on treatment or actively receiving ART in 2022, 12% ($n = 541$) transferred out, 14% ($n = 636$) defaulted or stopped treatment and 4% ($n = 182$) died (Table 1). Thirty-nine percent (1739) were diagnosed with HIV prior to their first birthday; the mean and median age at HIV diagnosis was 1 year old (interquartile range: 6 months–2 years). Over 90% ($n = 4150$) initiated ART within <14 days, and 80% initiated ART on the same day of diagnosis. Most children (58%) were asymptomatic at the time of their HIV diagnosis, but this proportion was lower in children who died (43%) compared to those who remained on treatment (61%). Among those who died, 50% ($n = 91$) did so within 6 months following their diagnosis and 92% ($n = 169$) died before the age of 2 years; age at diagnosis was similar between CLHIV <5 who died compared to all CLHIV <5 on ART. The proportion of CLHIV <5 who experienced delayed ART initiation (≥ 14 days after diagnosis) was similar among CLHIV who died (8%) compared to those who remained on treatment (7%) and those who transferred out (6%) or defaulted/stopped treatment (6%).

DISCUSSION

In 2022, 4% of CLHIV <5 on ART were reported to have died within Malawi's case surveillance system, though this number may be higher due to the percentage of CLHIV lost to follow-up as described below. Despite this possible limitation, these findings closely align with previously published global data showing that 4% of children <5 years old on ART died between 2004 and 2017⁵ and 3%–5% of CLHIV receiving ART in clinics supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) died from October 2020 to September 2022.³ The high percentage of CLHIV <5 that defaulted or stopped treatment (14%) is concerning, particularly the high rate of default among children ≤ 2 years of age, because the outcome of children who are lost to follow-up is often unknown and may include unreported deaths. Furthermore, others have reported that CLHIV <5 who are lost to follow-up may experience a higher risk of mortality.⁵

This analysis also found that only 39% of CLHIV on ART were diagnosed before their first birthday, likely reflecting gaps in antenatal and postnatal care of mothers living with HIV and their infants. However, most children had rapid ART initiation (within 14 days of diagnosis), indicating strong systems for ART linkage once diagnosed. Ensuring high coverage of early infant diagnosis and testing for HIV within the first 2 months of life have demonstrated substantial improvements in health outcomes and offer a better chance of survival.⁶

In addition, 43% CLHIV <5 who died were asymptomatic at the time of their HIV diagnosis and half died within 6 months following a diagnosis. These findings suggest that the first few months following an HIV diagnosis are critical, even if the infant appears to be in

good health at the time of their diagnosis. In alignment with World Health Organization recommendations, all newly diagnosed CLHIV <5 years old, even when they appear well, should be considered to have advanced HIV disease until stable on ART and at high risk for mortality and managed using the World Health Organization STOP AIDS Package.⁷

The findings in this report are subject to some limitations. First, clinic status was only available for the most recent entry, meaning that historical clinic status was replaced by new entries each time one was recorded. Therefore, longitudinal data regarding treatment status over time was not available for this analysis. Second, key contributors to mortality including malnutrition, immunizations, opportunistic infections and cause of death are not captured in Malawi's case surveillance system presently and could not be analyzed. Third, mortality may be underrepresented in our analysis as children lost to follow-up may have died but not been reported as deceased in the clinical record. Additionally, while Malawi does attempt to deduplicate data, it is possible that some records may be duplicated when transferring between facilities. Finally, ART regimen and viral load results could not be included in this analysis due to data quality issues.

Surveillance data are an important tool for managing a country's HIV epidemic, facilitating trend monitoring and preventing HIV-related mortality. Efforts to improve tracking, such as reporting clinical outcomes among children <5, can improve the capacity of governments to monitor the strengths and weaknesses of their programming. By leveraging HIV case surveillance data to identify and address gaps in care and treatment, public health initiatives can be better tailored to meet the specific needs of CLHIV, contributing to more effective prevention and intervention strategies.

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TABLE 1.

Demographic and Treatment Characteristics by Outcome Status in Children Living With HIV and on Antiretroviral Treatment Under the Age of 5 Years, Malawi, January–December, 2022

	On Treatment		Transferred Out		Defaulted or Treatment Stopped		Deceased		Total	
	n	%	n	%	n	%	n	%	n	%
Total	3102	69.5%	541	12.1%	636	14.3%	182	4.1%	4461	100.0%
Biological sex										
Female	1579	50.9%	280	51.8%	310	48.7%	92	50.5%	2261	50.7%
Male	1523	49.1%	261	48.2%	326	51.3%	90	49.5%	2200	49.3%
Age, yr										
0	122	3.9%	75	13.9%	94	14.8%	38	20.9%	329	7.4%
1	459	14.8%	124	22.9%	149	23.4%	57	31.3%	789	17.7%
2	798	25.7%	160	29.6%	191	30.0%	59	32.4%	1208	27.1%
3	990	31.9%	99	18.3%	126	19.8%	19	10.4%	1234	27.7%
4	733	23.6%	83	15.3%	76	11.9%	9	5.0%	901	20.2%
Age at HIV diagnosis, yr										
0	1228	39.6%	179	33.1%	254	39.9%	78	42.9%	1739	39.0%
1	1152	37.1%	152	28.1%	199	31.3%	64	35.2%	1567	35.1%
2	560	18.1%	141	26.1%	122	19.2%	29	15.9%	852	19.1%
3	144	4.6%	48	8.9%	48	7.5%	7	3.9%	247	5.5%
4	18	0.6%	21	3.9%	13	2.0%	4	2.2%	56	1.3%
WHO stage at diagnosis										
Stage 1: asymptomatic	1890	60.9%	296	54.7%	323	50.8%	78	42.9%	2587	58.0%
Stage 2: mild	72	2.3%	8	1.5%	18	2.8%	3	1.6%	101	2.3%
Stage 3: advanced	410	13.2%	84	15.5%	70	11.0%	20	11.0%	584	13.1%
Stage 4: severe	339	10.9%	86	15.9%	94	14.8%	44	24.2%	563	12.6%
Missing	391	12.6%	67	12.4%	131	20.6%	37	20.3%	626	14.0%
Timing of ART initiation										
Started same day	2494	80.4%	434	80.2%	493	77.5%	141	77.5%	3562	79.9%
Started within 2–13 d	378	12.2%	77	14.2%	107	16.8%	26	14.3%	588	13.2%
Delayed start ≥14 d	230	7.4%	30	5.6%	36	5.7%	15	8.2%	311	7.0%

	On Treatment		Transferred Out		Defaulted or Treatment Stopped		Deceased		Total	
	n	%	n	%	n	%	n	%	n	%
Time from HIV diagnosis to clinic outcome status										
<6 mo	128	4.1%	243	44.9%	254	39.9%	91	50.0%	716	16.1%
6 mo to <1 yr	587	18.9%	113	20.9%	119	18.7%	33	18.1%	852	19.1%
1 yr to <2 yr	1142	36.8%	121	22.4%	170	26.7%	45	24.7%	1478	33.1%
2 yr to <5 yr	1245	40.1%	64	11.8%	93	14.6%	13	7.1%	1415	31.7%

Comparison of children living with HIV under the age of 5 years by clinic status from January to December in 2022. Data pulled from Malawi's HIV case surveillance, which includes all individuals enrolled in care for HIV at ART clinics throughout the country.