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Death after discharge among children living with HIV admitted with suspected sepsis in Uganda: A secondary analysis of two prospective observational studies

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Abstract

Background: Children living with HIV in low-income countries contribute disproportionately to death after hospital discharge. This study investigates the effect of HIV on post-discharge mortality and readmission by exploring a wide range of clinical, maternal and socioeconomic variables.

Methods: A secondary analysis of children under 5 years old admitted with suspected sepsis. Participants were enrolled from two multisite observational studies conducted from 2012 to 2013 and 2017 to 2020 across six hospitals in Uganda. Participants were excluded if admitted outside the catchment area, for trauma, short-term observation or if admitted immediately after birth without prior discharge. We used a robust Poisson regression to identify risk factors of post-discharge mortality for three separate HIV groups: children living with HIV (CLHIV), children HIV-exposed uninfected (CHEU) and children HIV-unexposed uninfected (CHUU). We implemented Kaplan Meier curves to compare rates of post-discharge mortality and readmission between the three groups. In addition, we compared the risk ratio of the two outcomes.

Results: Of the 7658 children who were discharged alive and completed the 6-month follow-up, 266 (3.5%) were CLHIV, 458 (6.0%) were CHEU and 6934 (90.6%) were CHUU. Post-discharge mortality was statistically significantly higher in CLHIV compared to the CHUU, with rates of 12.8% (34/266) and

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5.8% (402/6934), respectively. Contrastingly, readmission was higher in CHUU (17.7% (1227/6934)) compared to CLHIV (11.3% (30/266)). Severe malnutrition, indicated by a weight-for-age z-score of less than −3, was associated with post-discharge mortality among all three groups with aRRs of 4.32 (95% CI: 1.89–9.81), 3.96 (95% CI: 1.75–8.95) and 4.84 (95% CI: 3.94–5.96) for CLHIV, CHEU and CHUU, respectively, compounded by the fact that severe malnutrition is disproportionately higher in those living with HIV. Variables associated with post-discharge mortality in this group were prior antimalarial use (aRR = 2.27 [95% CI: 1.16–4.47]) and moderate anaemia (aRR = 2.33 [95% CI: 1.12–4.89]).

Conclusions: Children living with HIV represent an exceptionally vulnerable group following hospital discharge. Very low readmission rates alongside high mortality suggest that strategies to improve care transitions and follow-up in these children are essential to improving recovery and survival.

KEYWORDS

HIV, mortality, paediatrics, post-discharge outcomes, readmission, sepsis

INTRODUCTION

Global child mortality has decreased by 52% since 2000, but progress has slowed in recent years, with 4.8 million children dying before reaching age 5 in 2023 [1]. One under-recognized contributor to child mortality in resource-poor settings is death following hospital discharge, which often exceeds in-hospital mortality rates [2]. This risk is especially pronounced among children recovering from severe acute illnesses like sepsis, with 50.8% of deaths occurring after hospital discharge [2]. This group frequently remains vulnerable to death for several months after leaving hospital care due to ongoing clinical, environmental and social challenges [2–5].

A recent systematic review and meta-analysis of 64 studies of paediatric post-discharge mortality in low- and middle-income countries identified several risk factors, including malnutrition, anaemia and human immunodeficiency virus (HIV) [6]. In children under 5 years of age, post-discharge deaths were higher among younger children and often occurred at home rather than after readmission to the hospital, underscoring systemic barriers to timely re-engagement with care. [2, 3]. Thus, there is a need to address both clinical vulnerabilities and health system deficiencies that perpetuate mortality after discharge.

HIV stands out among these risks. Despite the widespread adoption of antiretroviral therapy (ART), mortality among children living with HIV remains high, particularly in infants [7]. The meta-analysis by Knappett et al. [6] reported a pooled 6-month post-discharge mortality of 10.2% among children living with HIV in resource-poor settings. This is notably higher than the 4.4% mortality rate observed among children admitted with general acute illness [6]. These deaths underscore the need to address inadequate discharge planning for children living with HIV. A better understanding of modifiable comorbidities and systemic barriers to optimal care is necessary to guide informed decisions about the timing of discharge and the organization of post-discharge care.

Although sepsis is a leading cause of death among children living with HIV, little is known about this group's post-discharge trajectory and outcomes. Previous analyses from these cohorts focused on overall post-discharge mortality risk and modifiable factors among children admitted with suspected sepsis. This in-depth secondary analysis was conducted to better understand post-discharge outcomes among children living with HIV within the merged datasets. Children living with HIV represent a uniquely vulnerable population due to factors such as co-morbid illness, malnutrition, immunosuppression and challenges with long-term HIV care and antiretroviral adherence, all of which may contribute to higher mortality following hospital discharge.

Leveraging a large cohort of children enrolled with suspected sepsis, this study examines how HIV impacts post-discharge mortality and readmission and explores clinical, sociodemographic and health system factors that contribute to poor outcomes based on HIV status. Our analysis aims to inform strategies for improving post-discharge care and reducing preventable deaths in high-burden settings.

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METHODS

Study design

This secondary analysis leverages data from two prospective, multisite, observational cohort studies that have been previously described [2, 8]. The study enrolled participants aged 0 to 60 months admitted to six hospitals in Uganda with suspected sepsis and conducted a 6-month post-discharge follow-up to ascertain vital status and any attempts made to access healthcare. There were two separate enrollment periods from 2012 to 2013 and 2017 to 2020.

Study procedures

Participants were enrolled if they required admission for suspected sepsis. Suspected sepsis was defined as the need for admission due to a suspected or proven infection, which was previously demonstrated to be a pragmatic and effective criterion to capture sepsis using the International Paediatric Consensus Conference definition of paediatric sepsis [9, 10]. As most children admitted with a proven or suspected infection in this setting meet the International Paediatric Consensus Conference definition of paediatric sepsis [9] in our cohort [10], this approach captures a broader population of children at risk.

Exclusion criteria included living outside the catchment area, admission for trauma, short-term observation or admission immediately after birth without prior discharge. A positive HIV screening test was followed by a confirmatory rapid diagnostic test. Initial screening employed Determine (Abbott Point of Care) tests, with confirmatory testing using STAT-PAK and Uni-gold tests. Maternal HIV status was based on caregiver reports. No molecular testing results were captured for this analysis.

At admission, trained study nurses collected information on clinical variables, sociodemographic variables and baseline characteristics. Clinical data included anthropometry, vital signs, basic laboratory tests (haemoglobin status, malaria and HIV rapid tests), medical history (including antibiotic and antimalarial use as well as prior hospitalizations) and comorbidities. Sociodemographic data included sex, age, maternal characteristics (maternal age, education and HIV status), distance from facility, bed-net use and access to drinking water. Discharge type (routine, referral or unplanned) was recorded, as well as feeding status and discharge diagnosis.

Malnutrition was defined by the weight-for-age z-score (WAZ). A score of <-3 indicated severely underweight, -2 to -3 indicated underweight and > -2 indicated normal weight-for-age. Anaemia was defined based on haemoglobin concentration, with 7–10 g/dL indicating moderate anaemia and <7 g/dL indicating severe anaemia.

Participants were followed up by phone at two and four months and in person at six months post-discharge, all using the same standardized questionnaire to determine vital status and any engagement with the healthcare system, including readmissions. Verbal autopsies were conducted for those who died through a caregiver report.

All data were collected using encrypted tablets and stored securely in a centralized database.

Outcomes

For the present study, subjects were categorized into three groups: children living with HIV (CLHIV; defined as a positive RDT), children HIV-exposed uninfected (CHEU; defined by a negative RDT and self-reported maternal HIV infection) and children HIV-unexposed uninfected (CHUU). Participants without recorded HIV status or exposure status were excluded. The primary outcome of this analysis was post-discharge mortality within 6 months of hospital discharge. Secondary outcomes during the 6-month post-discharge period included readmission.

Statistical analysis

Descriptive statistics were used to quantify characteristics across HIV exposure groups. Categorical variables were summarized using counts and percentages, while continuous variables were reported using medians and interquartile ranges. Kaplan–Meier curves were used to compare post-discharge mortality and readmission over time between groups, with hazard proportionality assessed by analysis of scaled Schoenfeld residuals. To assess clinical and sociodemographic factors associated with 6-month post-discharge mortality, a Poisson regression model with robust standard error to estimate risk ratio was implemented, separately by HIV groups, adjusting for age, sex and site of enrollment. Adjustments for additional confounders were not done since this analysis was exploratory in nature, and we did not wish to build separate causal models for each clinical, social or laboratory feature and the outcome of interest. We conducted the regression analyses separately to account for potential effect modification by HIV status. This stratified approach allowed us to evaluate whether the strength and direction of associations between clinical/sociodemographic factors and outcomes differed according to HIV status. To examine the relationship between post-discharge mortality and readmission, the ratio of the two outcome rates was calculated

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by HIV status based on events per 1000 child-months from the date of index discharge.

All analyses were conducted using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and Stata/MP version 15.0 (StataCorp LLC, College Station, Texas, USA).

Ethical considerations

The original studies from which these data were derived were approved by the Mbarara University of Science and Technology Research Ethics Committee, the Uganda National Institute of Science and Technology and the University of British Columbia - Children and Women's Health Centre of British Columbia Research Ethics Board. Written informed consent was obtained from the parent or legal guardian of all study participants. This article follows the guidelines for Strengthening the Reporting and of Observational Studies in Epidemiology (STROBE) [11].

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation or writing of the report or in the decision to submit for publication.

RESULTS

A total of 21 650 children were screened, with 8813 (3688 (41.9%) aged 0 to less than 6 months and 5126 (58.2%) aged 6 to 60 months) enrolled. Of these, 594 (6.7%) had missing/unknown HIV status, 422 (4.8%) died in-hospital and 139 (1.6%) were lost to follow-up after discharge, resulting in 7658 children with complete 6-month follow-up and known HIV status (Figure 1). The final group comprised 266 (3.5%) CLHIV, 458 (6.0%) CHEU and 6934 (90.6%) CHUU (Figure 1). Of these participants, 1584 were enrolled in the 2012 to 2013 study [8], and 6074 were enrolled in the 2017 to 2020 study [2].

Post-discharge mortality rates were statistically significantly different (p-value <0.001) among the three HIV groups, with the highest rate among CLHIV at 12.8% (34/266), while both uninfected groups had similar rates at 5.7% (26/458) among CHEU and 5.8% (402/6934) among CHUU (Figure 2). Contrastingly, readmission rates observed the opposite phenomenon, with higher rates among CHUU (17.7% (1227/6934)) and CHEU (14.9% (68/458)) compared to CLHIV (11.3% (30/266)), and these differences were statistically significant (p-value = 0.01) (Figure 3). The readmission to post-discharge mortality rate ratios were lowest in CLHIV, with only 0.85 (95% CI: 0.52–1.40) readmissions to one mortality, compared to 2.73 (95% CI: 1.75–4.35) among

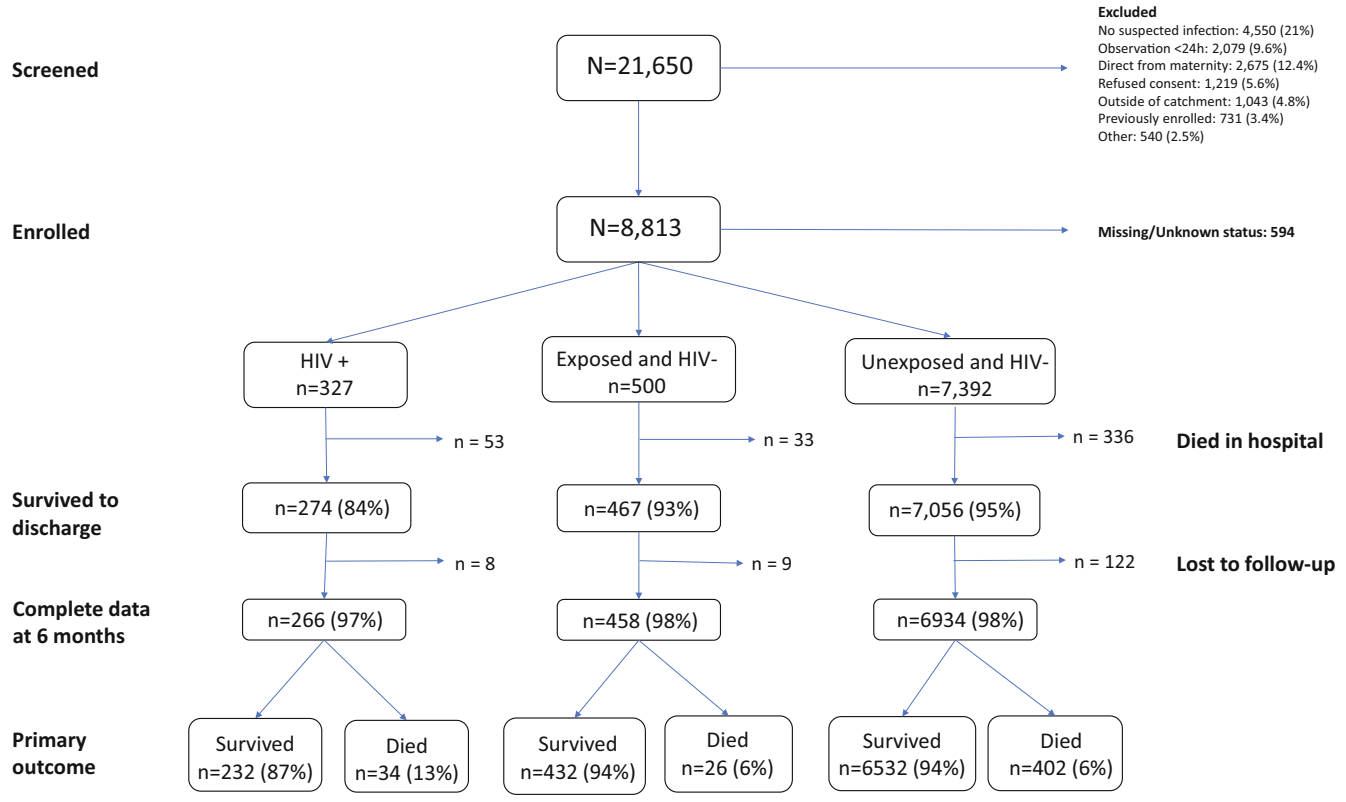


FIGURE 1 Flowchart of study participants.

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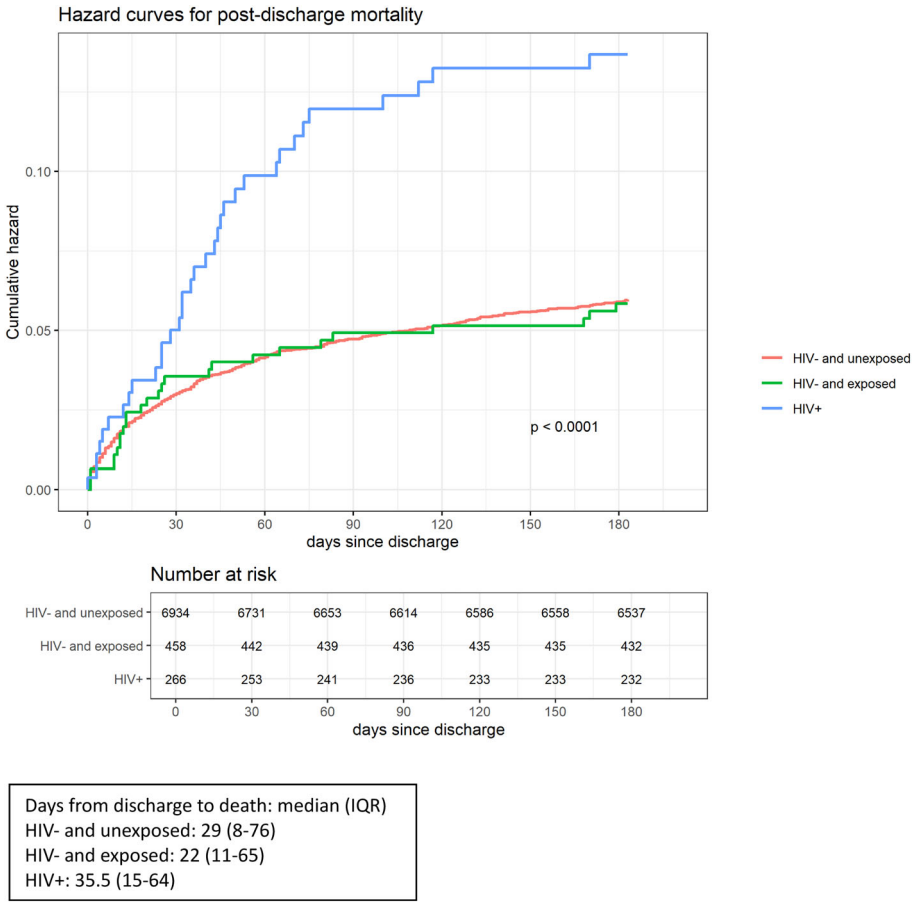


FIGURE 2 Hazard curves for post-discharge mortality by HIV status. *p*-value signifies statistical significance in the proportion of deaths between HIV groups. HIV, human immunodeficiency virus; IQR, interquartile range.

CHEU and 3.24 (95% CI: 2.90–3.63) readmissions per mortality event among CHUU (Figure 4).

Among the wide range of variables collected, severe malnutrition, as defined by a weight-for-age z-score less than −3, was strongly associated with post-discharge mortality across all three HIV groups after adjusting for age, sex and site. The aRRs were 4.32 (95% CI: 1.89–9.81), 3.96 (95% CI: 1.75–8.95) and 4.84 (95% CI: 3.94–5.96) among CLHIV, CHEU and CHUU, respectively (Table 1). In addition, children in the CLHIV group had a higher proportion of being severely malnourished at 39.1% (104/266) compared to 18.8% (86/458) among CHEU and 12.3% (852/6934) among CHUU. Mild to moderate anaemia was also more prevalent and significantly associated with mortality (aRR = 2.33 [95% CI: 1.12–4.89]), specifically among CLHIV after adjusting for age, sex and site. Prior antimalarial drug use was also significantly associated with post-discharge mortality among CLHIV (aRR = 2.27 [95% CI: 1.16–4.47]), but not among CHEU or CHUU after adjusting for age, sex and site. CLHIV were more likely to experience unplanned discharge (16.9% (45/266)) and had a higher proportion of post-discharge deaths occurring at home (67.6% (23/34)) (Table 2).

The five leading discharge diagnoses among CLHIV that were assigned by the clinical team were pneumonia (41.7% (111/266)), sepsis (21.4% (57/266)), malnutrition (21.4% (57/266)), gastroenteritis or diarrhoea (13.2% (35/266)) and tuberculosis (10.5% (28/266)) (Appendix Table S1a).

DISCUSSION

This study found that children living with HIV had more than double the rates of post-discharge mortality within 6 months compared to uninfected children. When comparing rates of readmission to post-discharge mortality, we found that HIV was substantially associated with lower rates of readmission despite having the highest rate of mortality during the post-discharge period. This finding provides a novel insight into the distinct post-discharge trajectory experienced by children living with HIV. Children living with HIV also had higher rates of post-discharge deaths occurring at home rather than during readmissions. These findings suggest that improved linkage with, and care within, community-based HIV

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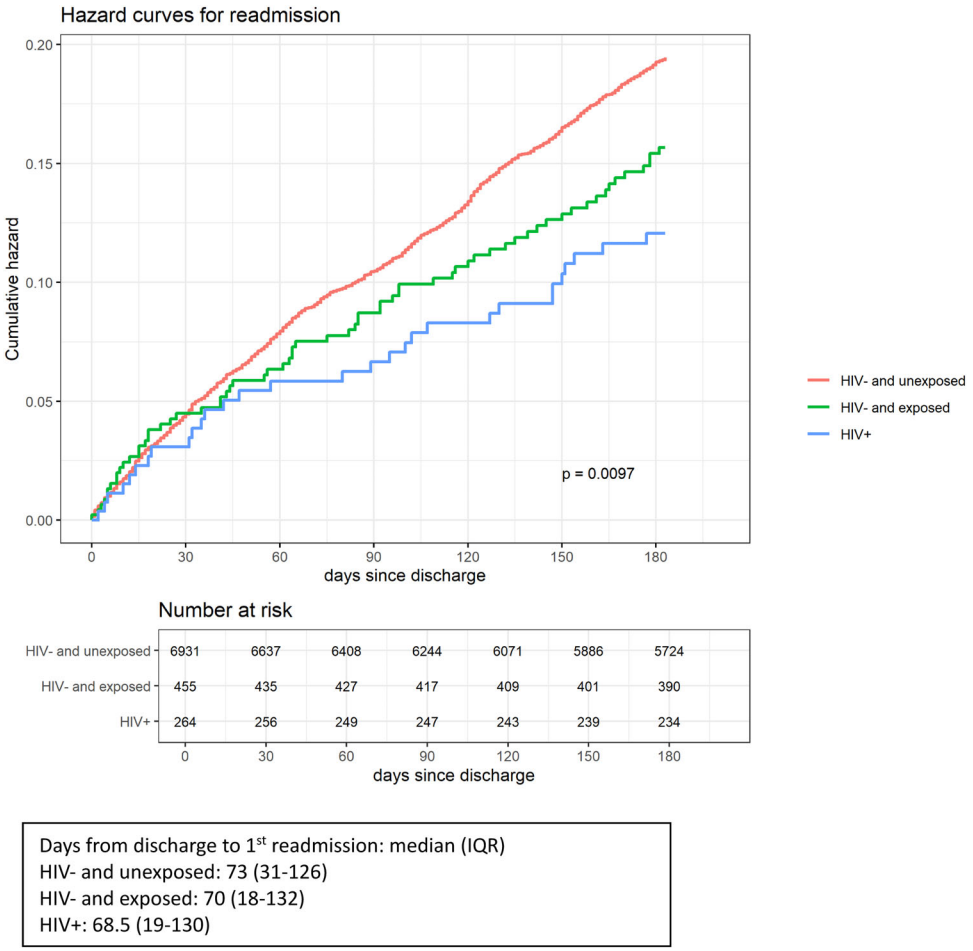


FIGURE 3 Hazard curves for readmission by HIV status. *p*-value signifies statistical significance in the proportion of deaths between HIV groups. HIV, human immunodeficiency virus; IQR, interquartile range.

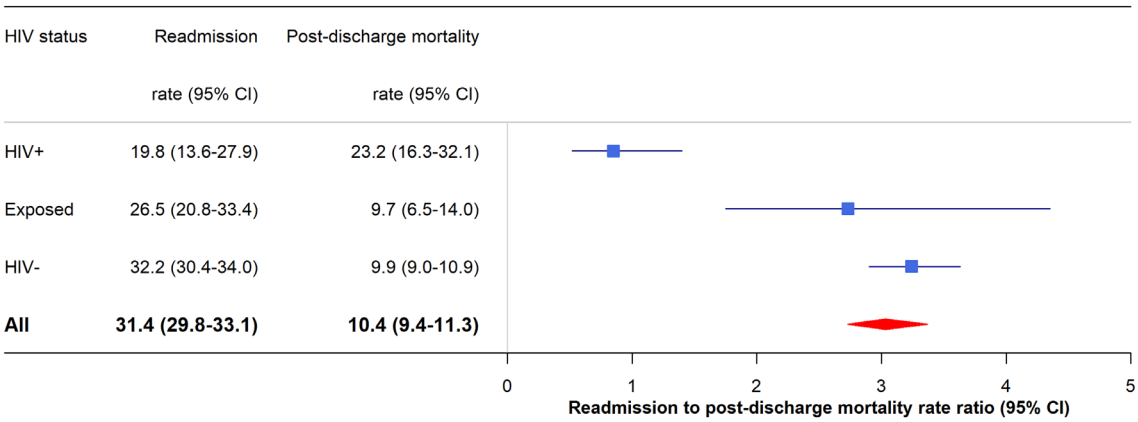


FIGURE 4 Comparing the rate of readmission with post-discharge mortality based on HIV status. Rates are per 1000 child-months, and arrows at the end of the line represent upper CI beyond the *x*-axis limit. CI, confidence interval; HIV, human immunodeficiency virus.

programs is critical to long-term recovery following acute illness in the context of HIV.

Our finding of higher post-discharge deaths in children living with HIV is not surprising in view of studies pointing out the effects of immunosuppression, comorbidities and suboptimal care transitions [2, 6, 12–14]. The improved access to antiretroviral therapy and prevention of mother-to-child transmission is an important advance in HIV care, but gains are likely to be derailed if we do not emphasize the need for longitudinal care, including post-

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TABLE 1 Comparison of demographic, maternal, social and clinical risk factors by HIV status.

	HIV+ ($N = 266$)		HIV− and exposed ($N = 458$)		HIV− and unexposed ($N = 6934$)	
	n **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**
Demographic variables						
Male Sex	146 (55.9)	0.85 (0.44–1.66)	237 (51.8)	2.46 (0.68–3.12)	3874 (55.9)	1.06 (0.87–1.28)
Age (years)	0.6 (0.2–1.6)	0.90 (0.70–1.15)	1.0 (0.4–2.0)	0.72 (0.43–1.20)	0.7 (0.2–1.5)	**0.98 (0.98–0.99)**
Admission Anthropometry						
MUAC (mm)	115 (102–132)	**0.97 (0.95–0.98)**	130 (115–145)	**0.96 (0.94–0.98)**	130 (114–144)	**0.96 (0.96–0.97)**
<110/<115	108 (40.6)	**3.89 (1.45–10.44)**	76 (16.6)	**6.25 (1.78–22.02)**	1380 (19.9)	**4.89 (3.70–6.48)**
110–120/115–125	61 (22.9)	2.14 (0.69–6.66)	102 (22.3)	**3.45 (1.03–11.54)**	1241 (17.9)	**2.31 (1.70–3.15)**
>120/>125	97 (36.5)	reference	280 (61.1)	reference	4313 (62.2)	reference
Weight for age Z-scores	−2.1 (−3.8–0.8)	**0.72 (0.64–0.82)**	−1.6 (−2.7 to −0.5)	**0.74 (0.63–0.87)**	−0.9 (−2.0–0.1)	**0.74 (0.71–0.76)**
<−3	104 (39.1)	**4.32 (1.89–9.81)**	86 (18.8)	**3.96 (1.75–8.95)**	852 (12.3)	**4.84 (3.94–5.96)**
−3 to −2	31 (11.7)	**3.15 (1.07–9.30)**	90 (19.7)	1.27 (0.39–4.13)	871 (12.6)	**2.67 (2.06–3.46)**
>−2	131 (49.3)	reference	282 (61.6)	reference	5211 (75.2)	reference
Admission Clinical Assessment						
Time since last admission						
Never	170 (63.9)	reference	306 (66.8)	reference	4751 (68.5)	reference
<1 month	9 (3.4)	1.24 (0.17–8.78)	16 (3.5)	**4.98 (1.81–13.67)**	265 (3.8)	**1.84 (1.23–2.74)**
1 month – 1 year	26 (9.8)	1.58 (0.56–4.47)	33 (7.2)	2.23 (0.74–6.73)	483 (7.0)	**2.33 (1.75–3.11)**
>1 year	58 (21.8)	1.80 (0.79–4.09)	103 (22.5)	0.22 (0.03–1.68)	1434 (20.7)	**1.32 (1.00–1.75)**
Referral	107 (40.2)	1.34 (0.71–2.52)	141 (30.8)	**2.48 (1.19–5.14)**	2204 (31.8)	**2.01 (1.66–2.44)**
Prior antibiotic use	129 (48.5)	1.13 (0.59–2.15)	193 (42.1)	0.84 (0.39–1.78)	3120 (45.0)	**1.34 (1.10–1.63)**
Prior antimalarial use	60 (22.6)	**2.27 (1.16–4.47)**	117 (25.6)	0.63 (0.21–1.86)	1664 (24.0)	1.15 (0.92–1.45)
Malaria test positive	27 (10.2)	1.25 (0.45–3.44)	94 (20.5)	0.41 (0.10–1.75)	1478 (21.3)	**0.66 (0.50–0.86)**
Haemoglobin status	11 (9.6–12.7)	-	11.7 (10–13.3)	-	12 (10–13.3)	-
Not anaemic (≥11 g/dL)	137 (51.9)	reference	276 (60.3)	reference	4256 (61.4)	reference
Mild to moderate anaemia (7–10 g/dL)	110 (41.7)	**2.33 (1.12–4.89)**	148 (32.3)	1.60 (0.75–3.40)	1983 (28.6)	1.12 (0.89–1.40)
Severe anaemia (<7 g/dL)	17 (6.4)	**4.62 (1.67–12.77)**	34 (7.4)	-	695 (10.0)	**2.28 (1.75–2.97)**
Maternal and Social Characteristics						
Time to reach the hospital						
<30 min	57 (21.4)	reference	123 (26.9)	reference	1559 (22.5)	reference
30 min–1 h	83 (31.2)	0.53 (0.21–1.37)	174 (38.0)	2.30 (0.60–8.80)	2357 (34.0)	1.34 (0.97–1.87)

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TABLE 1 (Continued)

	HIV+ ($N = 266$)		HIV− and exposed ($N = 458$)		HIV− and unexposed ($N = 6934$)	
	n **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**
1–2 h	89 (33.5)	0.81 (0.35–1.88)	114 (24.9)	**4.19 (1.13–15.61)**	2006 (28.9)	**2.36 (1.74–3.21)**
2–3 h	25 (9.4)	1.59 (0.08–4.32)	33 (7.2)	4.41 (0.83–23.52)	691 (10.0)	**2.38 (1.63–3.49)**
>3 h	12 (4.5)	0.60 (0.08–4.32)	14 (3.1)	3.50 (0.33–37.41)	321 (4.6)	**3.44 (2.26–5.25)**
Maternal age (years)	27 (23–30)	1.01 (0.96–1.07)	28 (25–33)	1.01 (0.94–1.08)	26 (23–30)	1.00 (0.98–1.02)
Maternal education						
No school/≤P3	46 (17.3)	reference	86 (18.8)	reference	751 (10.8)	reference
P4–P7	135 (50.8)	0.64 (0.29–1.41)	210 (45.9)	1.28 (0.43–3.77)	2849 (41.1)	**0.75 (0.57–0.98)**
S1–S6	63 (23.7)	0.59 (0.23–1.54)	130 (28.4)	0.93 (0.28–3.09)	2389 (34.5)	**0.55 (0.41–0.73)**
Post-Secondary	18 (6.8)	0.96 (0.29–3.21)	30 (6.6)	1.94 (0.43–8.88)	939 (13.5)	**0.38 (0.25–0.57)**
Maternal HIV status						
Negative	36 (13.5)	reference	-	-	-	-
Positive	205 (77.1)	0.98 (0.39–2.50)	-	-	-	-
Unknown	25 (9.4)	0.33 (0.04–2.93)	-	-	-	-
Bed net use						
Never	52 (19.6)	0.61 (0.21–1.81)	56 (12.2)	1.20 (0.43–3.29)	742 (10.7)	1.17 (0.87–1.58)
Sometimes	36 (13.5)	1.99 (0.83–4.77)	57 (12.5)	0.65 (0.15–2.94)	594 (8.6)	1.14 (0.82–1.60)
Always	178 (66.9)	reference	345 (75.3)	reference	5598 (80.7)	reference
Boil/disinfect/filter water	204 (76.7)	1.11 (0.44–2.83)	357 (78.0)	2.51 (0.71–8.94)	5062 (73.0)	**0.65 (0.52–0.80)**

Note: Categorical variables are presented using *n* (%) while continuous variables are presented in median (IQR). The aRRs were derived by fitting a robust Poisson regression model with post-discharge mortality as the outcome and variables in the first column as predictors while adjusting for age, sex and site of enrolment. Statistically significant aRRs are bolded. The lower cutoff for categorical MUAC is for children under 6 months old, while the higher cutoff is for 6–60 months old.

Abbreviations: aRR, adjusted risk ratio; BCS, Blantyre Coma Scale; CI, confidence interval; h, hours; HIV, human immunodeficiency virus; MUAC, middle-upper-arm circumference; P, primary school, where the following number represents school years; S, secondary school, where the following number represents school years; SpO2, oxygen saturation.

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TABLE 2 Comparison of discharge and post-discharge risk factors by HIV status.

	HIV+ (*N* = 266)		HIV− and exposed (*N* = 458)		HIV− and unexposed (*N* = 6934)	
	n **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**	***n*** **(%)/median (IQR)**	**aRR (95%CI)**
Length of stay (days)	6 (4–11)	1.02 (0.98–1.07)	4 (3–7)	1.01 (1.00–1.02)	**4 (3–6)**	**1.01 (1.01–1.02)**
Discharge status						
Routine discharge	212 (79.7)	reference	397 (86.7)	reference	5912 (85.3)	reference
Referred to higher level of care	9 (3.4)	**5.06 (1.97–12.99)**	11 (2.4)	**6.27 (1.97–19.95)**	239 (3.5)	**7.66 (6.05–9.69)**
Unplanned discharge	45 (16.9)	**3.65 (1.86–7.17)**	50 (10.9)	1.98 (0.80–4.90)	783 (11.3)	**3.49 (2.78–4.38)**
Feeding at discharge						
Feeding well	76 (28.6)	reference	101 (22.1)	reference	2259 (32.6)	reference
Feeding poorly	144 (54.1)	1.06 (0.48–2.32)	284 (62.0)	1.21 (0.47–3.10)	4201 (60.7)	**1.47 (1.17–1.84)**
Post-discharge mortality, *n* (%)	34 (12.8)	-	26 (5.7)	-	402 (5.8)	-
Location of death, *n* (%)						
At home	23 (67.6)	-	12 (46.2)	-	196 (48.8)	-
In-transit	1 (2.9)	-	4 (15.4)	-	69 (17.2)	-
At hospital	10 (29.4)	-	10 (38.5)	-	133 (33.1)	-

Note: Categorical variables are presented using *n* (%) while continuous variables are presented in median (IQR). The aRRs were derived by fitting a robust Poisson regression model with post-discharge mortality as the outcome and variables in the first column as predictors while adjusting for age, sex and site of enrolment. Statistically significant aRRs are bolded.

Abbreviations: aRR, adjusted risk ratio; CI, confidence interval; HIV, human immunodeficiency virus; IQR, interquartile range.

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discharge care. [2, 4]. Our study advances understanding of the burden incurred by HIV in young children and a catalogue of the comorbidities, such as malnutrition, anaemia, sepsis, lower respiratory tract infections and gastroenteritis, associated with increased vulnerability to death to inform post-discharge care.

Paediatric HIV is closely tied to nutritional deficiencies [3, 15, 16]. In this study, children living with HIV had the poorest nutritional status across all anthropometric measures, with two-thirds of children living with HIV classified as severely or moderately underweight at admission. HIV contributes to a decreased appetite, nutrient malabsorption and increased metabolic demands, which render recovery after discharge challenging [15, 17, 18]. These challenges are worsened by infection and sepsis, which negatively affect HIV-specific nutritional deficiency and together put this group further at a particularly high risk of death. In many LICs, these challenges are further compounded by food insecurity and limited access to nutritional support [18, 19]. Although the World Health Organization recommends that post-discharge care for children living with HIV explicitly address the burden of food insecurity [19], this remains difficult to achieve in resource-poor settings [18].

Lower respiratory tract infections (at discharge) and moderate anaemia (at admission) were more prevalent among children living with HIV. Both conditions have been established as indicators of poor prognosis in individuals living with HIV, especially when co-occurring alongside malnutrition [20–25]. Another important finding from our cohort was that malaria was much less common among children living with HIV. This is a promising finding, as HIV and malaria frequently co-occur in sub-Saharan Africa, where both are endemic [26]. The lower prevalence in our cohort may be a result of improved HIV care. At the same time, the correlation between prior antimalarial treatment and high mortality of children living with HIV suggests there may be a need to examine how febrile illness is managed in a malaria-endemic setting.

In our study, children living with HIV had 3-fold lower readmission-to-mortality ratios than those in the uninfected cohort. This raises concern that children living with HIV may face substantial barriers to timely reengagement with the healthcare system. Further supporting this assertion was the observation that a higher proportion of children living with HIV were found to be dying at home compared to the other uninfected cohorts. The poorer outcomes, even when hospital care is accessed, may be due to delayed presentation of acute illness, likely in extremis or possibly sub-optimal inpatient care. Further distances from the hospital were associated with a higher risk of post-discharge death for the uninfected cohorts but not among children living with HIV. This finding, alongside the lower readmission rates, indicates that children living with HIV may not seek hospital care even when critically ill.

Low rates of readmission may also be explained by barriers caregivers face in returning to care, including financial hardship (A. [5]), access to affordable and timely transportation, loss of faith in the healthcare system and unclear discharge instructions and arrangements for follow-up care [4, 27]. A qualitative study of the experiences of caregivers of children living with HIV in Uganda found that food insecurity and difficulties accessing healthcare posed major challenges for these families and that the lack of social protection programs further limited their ability to care for their child [28]. Delayed health seeking may also stem from caregivers' misperceptions of disease severity [4], which is also further complicated by HIV's variable presentation. Together, these findings may point to challenges in care-seeking after discharge as a contributor to mortality.

This study is subject to several limitations. First, the original studies were not designed to capture potentially relevant details related to HIV exposure confirmation, HIV treatment, treatment adherence, stage of disease and several other variables that would be critical to assessing the health and well-being of infants and children at risk or living with HIV infection. However, the large sample size provided important statistical strength to meaningfully evaluate the impact on post-discharge readmission and mortality within a general cohort of children admitted with suspected sepsis. Second, though the findings related to hospital readmission are very relevant, no data were captured on recurrent illness where health seeking was not sought, nor on motivations for health seeking, which are important to understand the dual nature of readmission as both an indicator of illness and of health seeking. Finally, this study was limited to multiple facilities in a single country. Future studies should assess the impact of HIV among children with suspected sepsis in other locations to further understand the wider implications of post-discharge mortality among children living with HIV, especially in Western and Central Africa, where there has been less of an international and domestic focus on HIV care [29]. Such studies should also examine differences in access to follow-up care and patterns of hospital readmission for this cohort.

CONCLUSION

In summary, children under five living with HIV in Uganda face markedly higher risks of post-discharge

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mortality. In our cohort, children living with HIV were less likely to be readmitted and more likely to die at home, indicating a greater need for careful pre-discharge planning and follow-up care post-discharge. Both acute care facilities and HIV treatment programs must recognize this and adapt their programs towards improving linkage, monitoring and care among children living with HIV who have recently been discharged from facilities.

AUTHOR CONTRIBUTIONS

MOW, NK and NF designed and conceptualized the study. JK, EK, CK, NKM and MOW contributed to data acquisition and supervision. CZ analysed the data. OM, MOW and NK drafted the manuscript. OM, NK, CZ, NF, NS, EK, JK, CK, NKM and MOW contributed to the interpretation of the data, critically reviewed the work for important intellectual content and agreed to be accountable for all aspects of the work. MOW is the guarantor.

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CONFLICT OF INTEREST STATEMENT

The authors do not have any conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request. Study materials, including the study protocol, consent form, data collection tools, de-identified participant data, data dictionary and the analysis code, will be available upon reasonable request to the corresponding author. Owing to the sensitive nature of clinical data, access to the de-identified data is granted on a case-by-case basis and will require the signing of a data sharing agreement.

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SUPPORTING INFORMATION

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