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Pneumonia and Malnutrition are Highly Predictive of Mortality among African Children Hospitalized with Human Immunodeficiency Virus Infection or Exposure in the Era of Antiretroviral Therapy

Geoffrey A. Preidis, PhD, **Eric D. McCollum, MD**, **Charles Mwansambo, MD**, **Peter N. Kazembe, MD**, **Gordon E. Schutze, MD**, and **Mark W. Kline, MD**

Interdepartmental Program in Translational Biology and Molecular Medicine, Department of Pediatrics (G.P.), Baylor International Pediatric AIDS Initiative Baylor College of Medicine, Texas Children's Hospital, (G.S., M.K.), Houston, TX; the Baylor International Pediatric AIDS Initiative, Baylor College of Medicine (E.M.), Department of Pediatrics, Kamuzu Central Hospital (C.M.), and the Baylor Children's Foundation-Malawi (P.K.), Lilongwe, Malawi

Abstract

Objective—To identify clinical characteristics predicting death among inpatients who are infected with or exposed to human immunodeficiency virus (HIV) during a period of pediatric antiretroviral therapy scale-up in sub-Saharan Africa.

Study design—Retrospective review of medical records from every child with HIV infection (n = 834) or exposure (n = 351) identified by routine inpatient testing in Kamuzu Central Hospital, Lilongwe, Malawi, September 2007 through December 2008.

Results—The inpatient mortality rate was high among children with HIV infection (16.6%) and exposure (13.4%). Clinically diagnosed *Pneumocystis* pneumonia or very severe pneumonia independently predicted death in inpatients with HIV infection (OR 14; 95% CI 8.2 to 23) or exposure (OR 21; CI 8.4 to 50). Severe acute malnutrition independently predicted death in children who are HIV infected (OR 2.2; CI 1.7 to 3.9) or exposed (OR 5.1; CI 2.3 to 11). Other independent predictors of death were septicemia, Kaposi sarcoma, meningitis, and esophageal candidiasis for children infected with HIV, and meningitis and severe anemia for inpatients exposed to HIV.

Conclusions—Severe respiratory tract infections and malnutrition are both highly prevalent and strongly associated with death among hospitalized children who are HIV infected or exposed. Novel programmatic and therapeutic strategies are urgently needed to reduce the high mortality rate among inpatients with HIV infection and HIV exposure in African pediatric hospitals.

Reprint requests: Geoffrey A. Preidis, PhD, Texas Children's Hospital; Feigin Center Suite 830; 1102 Bates Avenue; Houston, TX 77030. preidis@post.harvard.edu.

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Despite progress by developed nations in the prevention and treatment of pediatric human immunodeficiency virus (HIV), the number of children living with HIV worldwide (2.1 million) continues to rise. More than 430 000 children were newly infected, and 280 000 children died in 2008, totaling 16% of all new HIV infections and 14% of all HIV-attributable deaths globally. More than 90% of new infections and childhood deaths caused by HIV occurred in sub-Saharan Africa.[1]

Malawi is an African nation with an adult HIV prevalence of 12.7%.[1] National scale-up of pediatric antiretroviral therapy (ART) began in 2005, although the number of children receiving ART trails national goals.[2] In 2006, the Baylor College of Medicine-Abbott Fund Children's Clinical Centre of Excellence (COE) established a pediatric HIV outpatient clinic on the Kamuzu Central Hospital (KCH) campus in Lilongwe.[3] In 2007, COE clinicians began caring for inpatients who are HIV infected and HIV exposed at KCH. In 2008, the COE offered universal ART to identified Malawian infants younger than 1 year of age with HIV infection and began implementing a routine inpatient pediatric HIV testing program[4] that offered testing to approximately 80% of inpatients by the end of 2008.

Few studies have assessed inpatient pediatric HIV outcomes in the context of increasing ART in resource-constrained settings. This retrospective analysis describes the clinical characteristics of a cohort of 1235 hospitalized Malawian children with HIV infection or exposure, identifies predictors of death, and proposes strategies to reduce inpatient deaths associated with pediatric HIV in resource-limited settings.

Methods

The KCH pediatric ward is a crowded 215-bed referral facility averaging 42 and 34 daily admissions during the malaria and non-malaria seasons, respectively, for children <14 years of age. Data from every hospitalized inpatient with HIV infection and HIV exposure evaluated by an HIV-trained KCH clinician between September 1, 2007, and December 31, 2008, were recorded by COE pediatricians. The study was approved by the Malawi National Health Sciences Research Committee and Baylor College of Medicine institutional review boards.

KCH inpatients were referred to the HIV care team from the COE clinic, a hospital clinician, or an HIV counselor. HIV status was determined by antibody test if the child was >18 months, by antibody or DNA–polymerase chain reaction (PCR) test if the child was <18 months, or by presentation of valid prior HIV test results. Patients exposed to HIV were defined as being born to mothers infected with HIV, who were either without a definitive HIV test result or were HIV DNA-PCR– negative but breastfeeding. Children initially identified as HIV-exposed were reidentified as HIV-infected if their DNA-PCR test result was positive.

Each child was evaluated by a clinician trained in the treatment of pediatric HIV.[5] At discharge, clinicians recorded up to six diagnoses by use of World Health Organization (WHO) and Malawi Ministry of Health criteria,[6, 7] as well as a WHO clinical stage if the child was infected with HIV. Malaria and bacterial meningitis diagnoses included both

laboratory-positive and suspected cases.[7] The study was conducted within the context of standard inpatient care; thus definitive diagnostic tests were unavailable for *Pneumocystis* pneumonia (PCP), sepsis, pulmonary/extrapulmonary tuberculosis, and esophageal candidiasis. These diagnoses represented suspected cases on the basis of current guidelines. [6, 7] Suspected cases also included patients with missing laboratory results or with early treatment precluding definitive laboratory diagnoses. At discharge, patients not receiving outpatient care at the COE were offered referral.

Statistical Analyses

Non-parametric continuous variables were evaluated by Mann-Whitney U test and categorical variables were evaluated with Pearson χ^2 or Fisher exact tests to assess bivariate associations for each variable with the dependent variable, death in the hospital. Binary logistic regression was used to calculate unadjusted ORs and 95% CIs. To identify independent predictors of mortality, covariates with P <.10 in bivariate analysis were used to create multivariate logistic regression models. Variables were entered into the analysis by forward stepwise selection, with entry testing based on the significance of the score statistic and removal testing based on the probability of a likelihood-ratio statistic with conditional parameter estimates. Hosmer-Lemeshow goodness-of- fit statistics confirmed that the final models adequately fit each data set. All statistical analyses were performed using SPSS software (version 17.0; SPSS Inc, Chicago, Illinois).

Results

During the 16-month study period, 15 271 children were admitted to KCH, and routine HIV testing identified 884 inpatients with HIV infection and 351 inpatients with HIV exposure (Table I). Although the overall mortality rate at KCH was 7.3%, the mortality rate was especially high in children who were HIV infected (16.6%) and HIV exposed (13.4%), and although the median duration between hospital admission and death at KCH was 2 days, most deaths in cohorts with HIV infection and HIV exposure occurred nearly 1 week after hospital admission. Low cluster of differentiation 4 (CD4) laboratory values correlated with advanced WHO stage (77% stage III/IV), and one in four children infected with HIV was receiving ART (median duration 3.3 months; 90.3% first-line therapy). The most prevalent diagnoses were severe pneumonia (39.8%), sepsis (34.4%), severe acute malnutrition (SAM; 30.8%), gastroenteritis (26.5%), and malaria (24.2%). Children with HIV exposure had lower rates of severe pneumonia, SAM, pulmonary tuberculosis, esophageal candidiasis, and Kaposi sarcoma, and higher rates of sepsis and gastroenteritis, compared with children with HIV infection (P < .05). Twenty-six cases of Kaposi sarcoma were identified, mostly in children with HIV infection, median age 66 months.

Bivariate analysis revealed unadjusted ORs for factors predictive of death in children who were HIV-infected (Table II). WHO stage IV, very severe pneumonia, clinically diagnosed PCP, SAM, sepsis, Kaposi sarcoma, and esophageal candidiasis correlated with greater inpatient mortality (P < .05). Potential correlations (P < .10) included WHO stage III, decreasing CD4 percent, and bacterial meningitis. Neither ART usage nor adherence correlated with increased survival. Multivariate analysis determined independent predictors

of inpatient death within this cohort. Very severe pneumonia and clinically diagnosed PCP were strongly collinear; thus, they were combined into a single predictor. Although malaria was associated with a decreased mortality rate in bivariate analysis, this correlation was presumably due to high hospital prevalence and availability of effective therapy, rather than biologic protection from death. Thus, malaria was excluded from multivariate models. CD4 percent was excluded due to the number of missing values. In multivariate analyses, clinically diagnosed PCP or very severe pneumonia, sepsis, SAM, Kaposi sarcoma, bacterial meningitis, and esophageal candidiasis were positive predictors of in-hospital death. However, neither WHO stage III/IV nor WHO stage IV alone independently predicted death in children infected with HIV.

Unadjusted and adjusted ORs also were determined for clinical characteristics predicting mortality among inpatients with HIV exposure (Table III). All four variables entered into the multivariate model independently predicted death in children exposed to HIV, namely clinically diagnosed PCP or very severe pneumonia, SAM, bacterial meningitis, and severe anemia. Clinically diagnosed PCP or very severe pneumonia was an especially strong independent predictor of death, with an adjusted OR 14 (95% CI 8.2 to 23; $P < .001$) for children with HIV infection, and OR 21 (CI 8.4 to 50; $P < .001$) for children with HIV exposure. Likewise, the adjusted OR for the relationship between SAM and inpatient death was 2.5 (CI 1.7 to 3.9; $P < .001$) for children infected with HIV and 5.1 (CI 2.3 to 11; $P < .001$) for infants exposed to HIV.

Discussion

From the beginning of the global scale-up of ART, children have been underrepresented as recipients of both HIV care and treatment.[8] Most African children first gain access to HIV care in pediatric hospitals,[4, 9] which face high burdens of HIV-related admissions and death.[10] However, little is known about pediatric inpatients in the era of ART, and it is not yet known whether specific clinical features might predict which children who were infected or exposed to HIV are at especially high risk for poor hospital outcomes. To address this knowledge gap, we used multivariate regression analysis to identify six independent predictors of death among 884 hospitalized children with HIV infection and four independent predictors of hospital death among 351 children with HIV exposure. Very severe pneumonia and SAM were highly prevalent and strongly predictive of death in both inpatient cohorts. These data reveal important targets for immediate improvement of hospital-based pediatric HIV care.

Our analyses revealed that the clinical characteristic most predictive of death among hospitalized children with HIV infection and HIV exposure was clinically diagnosed PCP or very severe pneumonia. Lower respiratory tract infections were extremely common in our inpatient cohorts, confirming prior community-based analyses in southern Africa.[11] A high inpatient mortality rate attributed to PCP was reported before ART introduction[12] and more recently in a South African pediatric hospital.[13] Our data extend these findings, revealing that clinically diagnosed PCP or very severe pneumonia is the strongest predictor of death for inpatients with both HIV infection and HIV exposure in the era of pediatric ART.

At KCH, the high mortality rate from clinically diagnosed PCP or very severe pneumonia may reflect inadequate access to oxygen, bacteriologic culture, antimicrobial agents, and unavailability of mechanical ventilation. Radiography was available for chest imaging, although access was limited, and children receiving oxygen from immobile concentrator machines could not be safely transported to the radiology department. Ultrasonography was rare, and portable and lateral radiography and chest computed tomography were unavailable. Acritically low nurse-to-patient ratio further limited provision of basic respiratory care. Although specific pathogens could not be identified, recent studies in South Africa found viral, fungal, mycobacterial, bacterial, and polymicrobial infections to be common causes of severe and very severe pneumonia in children with HIV infection and HIV exposure.[14] Some forms of pneumonia were likely misdiagnosed because of limited diagnostic capabilities. Cytomegalovirus, tuberculosis, and *Pneumocystis* infection were common in children infected with HIV with fatal acute respiratory disease in Zambia[15]; use of oral corticosteroids for children with HIV infection incorrectly diagnosed with PCP might compromise treatment response to tuberculosis or cytomegalovirus. Pulmonary tuberculosis likely was underdiagnosed; studies in HIV-endemic settings show that clinical criteria alone often miss this disease.[16]

SAM is also strongly predictive of inpatient death. This finding supports prospective studies indicating that children infected with HIV have a threefold higher mortality rate during nutritional rehabilitation compared with uninfected children,[17–19] and we extend these results to the pediatric hospital and to infants exposed to HIV. SAM presents an array of unique challenges with children with HIV-infection.[20] For example, even after nutritional rehabilitation, CD4 levels continue to fall until ART is initiated.[21] At KCH, some SAM diagnoses were likely undernutrition caused by coinfection with unidentified tuberculosis.[22] Other inpatients might have had wasting caused by occult cancer. Malignancy is highly prevalent in children with HIV infection,[23] and more than half of Malawian children with cancer meet diagnostic criteria for SAM.[24] Future studies must identify when ART should be initiated for children receiving nutritional rehabilitation.

Children exposed to HIV admitted to the hospital had unexpectedly high inpatient mortality rates. We found similar inpatient mortality rates between children with HIV exposure and HIV infection, even after controlling for age. For children exposed to HIV, high morbidity and mortality rates could reflect socioeconomic circumstances (eg, poor health status of the mother) or undiagnosed HIV infection (eg, infants too sick to be transported to HIV testing rooms). Furthermore, 9% of infants with HIV exposure were too young for initiation of cotrimoxazole preventive therapy and thus were at increased risk for acquiring PCP. Infants with HIV exposure had similar rates of pneumonia, malaria, severe anemia, and bacterial meningitis compared with children with HIV infection. However, infants exposed to HIV had higher rates of gastroenteritis and sepsis; the former could be due to younger age, and the latter might be due to less frequent use of cotrimoxazole preventive therapy among infants with HIV exposure. Not surprisingly, gastroenteritis was diagnosed less often in breastfed infants (23.9 vs 34.7%; $P = .031$). Lower rates of SAM among children with HIV exposure, compared with those infected with HIV, could be attributed to their uninfected

status. Additional research is needed to more completely understand the challenging clinical spectra of uninfected children with HIV exposure in the inpatient setting.

Among our study's limitations, definitive diagnoses such as PCR-positive PCP and culture-positive bacteremia were unavailable, and CD4 values could be obtained only for a subset of patients. Resource constraints, which limited the depth to which we could describe these patients, reflect real diagnostic challenges for pediatricians serving in African hospitals. Furthermore, children with HIV infection receiving ART had only been on therapy for a median of 3 months; thus they might differ from pediatric cohorts receiving ART for longer durations. Finally, the infant cohort exposed to HIV might have included inpatients with undiagnosed HIV infection, and just 48% children with HIV exposure had documented negative DNA-PCR test results. This situation also reflects the challenges of HIV testing in the midst of routine inpatient care in most resource-constrained African hospitals.

Clinicians providing care for African children with HIV infection and HIV exposure must be aware that both cohorts have high in-hospital mortality rates, and that severe respiratory tract infections and SAM are common and highly predictive of death. Thus we recommend urgent investigation of novel approaches that maximize material and human resources for inpatient acute respiratory support and nutritional rehabilitation. Novel programmatic and therapeutic strategies, including revision of inpatient clinical guidelines, could catalyze reduction of mortality among hospitalized children with HIV infection and HIV exposure. However, these approaches must take into account critical knowledge gaps and profound resource constraints. Inpatient HIV diagnosis and care will need to be prioritized for a rapid global scale-up of pediatric ART to be successful.

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Glossary

ART	Antiretroviral therapy
CD4	Cluster of differentiation 4
COE	Baylor College of Medicine-Abbott Fund Children's Clinical Centre of Excellence
HIV	Human immunodeficiency virus
KCH	Kamuzu Central Hospital
PCP	*Pneumocystis* pneumonia
PCR	Polymerase chain reaction
SAM	Severe acute malnutrition
WHO	World Health Organization

References

1. Joint United Nations Program on HIV/AIDS/World Health Organization (UNAIDS/WHO). AIDS epidemic update 2009. Geneva: UNAIDS/WHO; 2009.
2. Malawi Paediatric Antiretroviral Treatment Group. Antiretroviral therapy for children in the routine setting in Malawi. Trans R Soc Trop Med Hyg. 2007; 101:511–516. [PubMed: 17197006]
3. Kabue MM, Chitsulo C, Kazembe PN, Mizwa MB, Calles NR. A paediatric HIV care and treatment programme in Malawi. Malawi Med J. 2008; 20:19–22. [PubMed: 19260442]
4. McCollum ED, Preidis GA, Kabue MM, Singogo EB, Mwansambo C, Kazembe PN, et al. Task shifting routine inpatient pediatric HIV testing improves program outcomes in urban Malawi: a retrospective observational study. PLoS One. 2010; 5:e9626. [PubMed: 20224782]
5. Kline MW, Ferris MG, Jones DC, Calles NR, Mizwa MB, Schwarzwald HL, et al. The Pediatric AIDS Corps: responding to the African HIV/AIDS health professional resource crisis. Pediatrics. 2009; 123:134–136. [PubMed: 19117871]
6. World Health Organization (WHO) HIV/AIDS Programme. Antiretroviral therapy for HIV infection in infants and children: towards universal access. Geneva: WHO; 2010.
7. Malawi Ministry of Health National AIDS Commission. Management of HIV-related diseases. Lilongwe, Malawi: Malawi Ministry of Health; 2008.
8. Kline MW. Perspectives on the pediatric HIV/AIDS pandemic: catalyzing access of children to care and treatment. Pediatrics. 2006; 117:1388–1393. [PubMed: 16585337]
9. Kankasa C, Carter RJ, Briggs N, Bulterys M, Chama E, Cooper ER, et al. Routine offering of HIV testing to hospitalized pediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility. J Acquir Immune Defic Syndr. 2009; 51:202–208. [PubMed: 19504732]
10. Rogerson SR, Gladstone M, Callaghan M, Erhart L, Rogerson SJ, Borgstein E, et al. HIV infection among paediatric in-patients in Blantyre, Malawi. Trans R Soc Trop Med Hyg. 2004; 98:544–552. [PubMed: 15251404]
11. Obimbo EM, Mbori-Ngacha DA, Ochieng JO, Richardson BA, Otieno PA, Bosire R, et al. Predictors of early mortality in a cohort of human immunodeficiency virus type 1-infected african children. Pediatr Infect Dis J. 2004; 23:536–543. [PubMed: 15194835]
12. Graham SM, Mtitimila EI, Kamanga HS, Walsh AL, Hart CA, Molyneux ME. Clinical presentation and outcome of Pneumocystis carinii pneumonia in Malawian children. Lancet. 2000; 355:369–373. [PubMed: 10665557]
13. Morrow BM, Hsaio NY, Zampoli M, Whitelaw A, Zar HJ. Pneumocystis pneumonia in South African children with and without human immunodeficiency virus infection in the era of highly active antiretroviral therapy. Pediatr Infect Dis J. 2010; 29:535–539. [PubMed: 20072079]
14. McNally LM, Jeena PM, Gajee K, Thula SA, Sturm AW, Cassol S, et al. Effect of age, polymicrobial disease, and maternal HIV status on treatment response and cause of severe pneumonia in South African children: a prospective descriptive study. Lancet. 2007; 369:1440–1451. [PubMed: 17467514]
15. Chintu C, Mudenda V, Lucas S, Nunn A, Lishimpi K, Maswahu D, et al. Lung diseases at necropsy in African children dying from respiratory illnesses: a descriptive necropsy study. Lancet. 2002; 360:985–990. [PubMed: 12383668]
16. Edwards DJ, Kitetele F, Van Rie A. Agreement between clinical scoring systems used for the diagnosis of pediatric tuberculosis in the HIV era. Int J Tuberc Lung Dis. 2007; 11:263–269. [PubMed: 17352090]
17. Sadler K, Kerac M, Collins S, Khengere H, Nesbitt A. Improving the management of severe acute malnutrition in an area of high HIV prevalence. J Trop Pediatr. 2008; 54:364–369. [PubMed: 18450820]
18. Chinkhumba J, Tomkins A, Banda T,Mkangama C, Fergusson P. The impact of HIV on mortality during in-patient rehabilitation of severely malnourished children in Malawi. Trans R Soc Trop Med Hyg. 2008; 102:639–644. [PubMed: 18534649]

19. Fergusson P, Chinkhumba J, Grijalva-Eternod C, Banda T, Mkangama C, Tomkins A. Nutritional recovery in HIV-infected and HIV-uninfected children with severe acute malnutrition. Arch Dis Child. 2009; 94:512–516. [PubMed: 18977785]

20. Heikens GT, Bunn J, Amadi B, Manary M, Chhagan M, Berkley JA, et al. Case management of HIV-infected severely malnourished children: challenges in the area of highest prevalence. Lancet. 2008; 371:1305–1307. [PubMed: 18406865]

21. Hughes SM, Amadi B, Mwiya M, Nkamba H, Mulundu G, Tomkins A, et al. CD4 counts decline despite nutritional recovery in HIV-infected Zambian children with severe malnutrition. Pediatrics. 2009; 123:e347–e351. [PubMed: 19124582]

22. Kessler L, Daley H, Malenga G, Graham S. The impact of the human immunodeficiency virus type 1 on the management of severe malnutrition in Malawi. Ann Trop Paediatr. 2000; 20:50–56. [PubMed: 10824214]

23. Mueller BU. Cancers in children infected with the human immunodeficiency virus. Oncologist. 1999; 4:309–317. [PubMed: 10476542]

24. Israels T, Chirambo C, Caron HN, Molyneux EM. Nutritional status at admission of children with cancer in Malawi. Pediatr Blood Cancer. 2008; 51:626–628. [PubMed: 18668514]

Table I

Characteristics of inpatients studied

Characteristic	HIV infection (n = 884)	HIV exposure (n = 351)
Age, median months ± IQR	21.8 (11.1–44.6)	7.4 (2.6–11.3)
Female, n (%)	405 (45.8)	174 (49.6)
Died in hospital, n (%)	147 (16.6)	47 (13.4)
Age at death, median months ± IQR	18.5 (9.4–38.6)	8.6 (4.7–12.8)
Time from admission to death, median days ± IQR	6 (4–10)	5 (3–10)
CD4 cells*		
Percent, mean (SD)	20.0 (10.0)	—
Absolute, mean (SD)	315.2 (333.6)	—
WHO stage I/II/III/IV	86/117/398/283 (9.7%/13.2%/45.0%/32.0%)	—
Diagnoses		
Severe pneumonia	371 (42.0%)	121 (34.5%)
Very severe pneumonia	102 (11.5%)	33 (9.4%)
Pneumocystis pneumonia	69 (7.8%)	21 (6.0%)
Severe acute malnutrition	313 (35.4%)	67 (19.1%)
Sepsis	275 (31.1%)	150 (42.7%)
Malaria	217 (24.5%)	82 (23.4%)
Gastroenteritis	206 (23.3%)	121 (34.5%)
Pulmonary tuberculosis	99 (11.2%)	15 (4.3%)
Severe anemia	45 (5.1%)	15 (4.3%)
ART toxicity	11 (5.1%)†	—
Bacterial meningitis	35 (4.0%)	12 (3.4%)
Esophageal candidiasis	35 (4.0%)	6 (1.7%)
Kaposi sarcoma	25 (2.8%)	1 (0.2%)
Extrapulmonary tuberculosis	15 (1.7%)	1 (0.3%)

*448 children <5 years with CD4 percent and 134 children >5 years with absolute CD4 during admission.

†Percent of children on ART (n = 217); toxicities included lactic acidosis (n = 6), Stevens Johnson syndrome (n = 3), and pancreatitis (n = 2).

Table II

Predictors of mortality for inpatients infected with HIV

Characteristic	Bivariate analysis				Multivariate analysis		
	Died in hospital (n = 147)	Discharged alive (n = 737)	OR (95% CI)	*P* value	Wald statistic*	OR (95% CI)	*P* value
Diagnosis,							
Severe pneumonia	59 (40.1%)	312 (42.3%)	0.91 (0.64–1.3)	.622			
Very severe pneumonia	57 (38.8%)	45 (6.1%)	9.7 (6.2–15)	<.001	103.1	14 (8.2–23)	<.001
Pneumocystis pneumonia	23 (15.6%)	46 (6.2%)	2.8 (1.6–4.8)	<.001			
Severe acute malnutrition	72 (49.0%)	241 (32.7%)	2.0 (1.4–2.8)	<.001	18.84†	2.5 (1.7–3.9)	<.001
Sepsis	70 (47.6%)	205 (27.8%)	2.4 (1.6–3.4)	<.001	27.03	3.1 (2.0–4.7)	<.001
Malaria	20 (13.6%)	197 (26.7%)	0.43 (0.26–0.71)	.001			
Gastroenteritis	38 (25.9%)	168 (22.8%)	1.2 (0.79–1.8)	.424			
Pulmonary tuberculosis	16 (10.9%)	83 (11.3%)	0.96 (0.55–1.7)	.895			
Kaposi sarcoma	8 (5.4%)	17 (2.3%)	2.4 (1.0–5.8)	.042	12.77	6.2 (2.3–17)	<.001
Severe anemia	9 (6.1%)	36 (4.9%)	1.3 (0.60–2.7)	.534			
ART toxicity	2 (5.9%)	9 (4.9%)	1.2 (0.25–5.9)	.814			
Bacterial meningitis	10 (6.8%)	25 (3.4%)	2.1 (0.98–4.4)	.058	8.474	3.5 (1.5–8.3)	.004
Extrapulmonary tuberculosis	2 (1.4%)	13 (1.8%)	0.77 (0.17–3.4)	.730			
Esophageal candidiasis	13 (8.8%)	22 (3.0%)	3.2 (1.6–5.4)	.002	4.481	2.5 (1.1–5.6)	.034
Age, median months ± IQR	18.5 (9.4–38.6)	22.4 (11.5–46.3)	—	.471			
Female sex	68 (46.3%)	337 (45.7%)	1.0 (0.72–1.5)	.906			
ART status							
On ART	34 (23.1%)	183 (24.8%)	0.91 (0.60–1.4)	.662			
History of ART toxicity	3/34 (8.8%)	7/183 (3.8%)	2.4 (0.60–9.9)	.215			
Adherence <95% or >105%	8/34 (23.5%)	53/183 (29.0%)	0.76 (0.32–1.8)	.519			
CD4‡							
Percent, mean ± SD	17.9 (9.6)	20.3 (10.0)	—	.095			
Absolute, mean ± SD	194.1 (231.8)	331.9 (342.8)	—	.124			
WHO stage							
I	5 (3.4%)	81 (11.0%)	Reference				

Characteristic	Bivariate analysis				Multivariate analysis		
	Died in hospital (n = 147)	Discharged alive (n = 737)	OR (95% CI)	*P* value	Wald statistic*	OR (95% CI)	*P* value
II	13 (8.8%)	104 (14.1%)	2.0 (0.69–5.9)	.197			
III	51 (34.7%)	347 (47.1%)	2.4 (0.92–6.2)	.073			
IV	78 (53.1%)	205 (27.8%)	6.2 (2.4–16)	<.001	1.675§	—	.196

*Score statistic is reported instead of Wald statistic for predictors not fitting in final multivariate model.

†Pneumocystis and very severe pneumonia were strongly colinear; thus, they were combined into a single predictor for multivariate analysis.

‡CD4 percent was available for 56 in the died in hospital group and 396 in the discharged alive group. Absolute CD4 was available for 15 in the died in hospital group and 109 in the discharged alive group.

§Neither WHO stage III/IV combined (shown) nor WHO stage IV alone independently predicted death.

Table III

Predictors of death for inpatients exposed to HIV

Characteristic	Bivariate analysis				Multivariate analysis		
	Died in hospital (n = 47)	Discharged alive (n = 304)	OR (95% CI)	*P* value	Wald statistic	OR (95% CI)	*P* value
Diagnosis, n (%)							
Severe pneumonia	20 (42.6%)	101 (33.2%)	1.5 (0.80–2.8)	.212			
Very severe pneumonia	20 (42.6%)	13 (4.3%)	17 (7.4–37)	<.001	43.73	21 (8.4–50)	<.001
Pneumocystis pneumonia	8 (17.0%)	13 (4.3%)	4.6 (1.8–12)	.002			
Severe acute malnutrition	20 (42.6%)	47 (15.5%)	4.1 (2.1–7.8)	<.001	16.52*	5.1 (2.3–11)	<.001
Sepsis	25 (53.2%)	125 (41.1%)	1.6 (0.88–3.0)	.122			
Malaria	6 (12.8%)	76 (25.0%)	0.44 (0.18–1.1)	.071			
Gastroenteritis	21 (44.7%)	100 (32.9%)	1.6 (0.88–3.1)	.116			
Pulmonary tuberculosis	2 (4.3%)	13 (4.3%)	1.0 (0.22–4.6)	.995			
Kaposi sarcoma	0 (0.0%)	1 (0.3%)	—				
Severe anemia	6 (12.8%)	9 (3.0%)	4.8 (1.6–14)	.005	5.294	4.9 (1.3–19)	.021
Bacterial meningitis	4 (8.5%)	8 (2.6%)	3.4 (0.99–1.2)	.051	6.899	7.0 (1.6–30)	.009
Extrapulmonary tuberculosis	1 (2.1%)	0 (0.0%)	—				
Esophageal candidiasis	2 (4.3%)	4 (1.3)	3.3 (0.59–19)	.172			
Age, median months ± IQR	8.6 (4.7–12.8)	7.3 (2.5–11.2)	—	.101			
Female sex	28 (59.6%)	146 (48.0%)	1.6 (0.85–3.0)	.143			
Breastfed within 6 weeks	32 (68.1%)	222 (73.0%)	0.79 (0.41–1.5)	.482			

*Pneumocystis and very severe pneumonia were strongly colinear; thus they were combined into a single predictor for multivariate analysis.