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Routine Inpatient Provider-Initiated HIV Testing in Malawi, Compared to Client-Initiated Community-Based Testing, Identifies Younger Children at Higher Risk of Early Mortality

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Abstract

Objective—Determine how routine inpatient provider-initiated HIV testing differs from traditional community-based client-initiated testing with respect to clinical characteristics of children identified and outcomes of outpatient HIV care.

Design—Prospective observational cohort.

Methods—Routine clinical data were collected from children identified as HIV-infected by either testing modality in Lilongwe, Malawi in 2008. After one year of outpatient HIV care at the Baylor College of Medicine Clinical Center of Excellence, outcomes were assessed.

Results—Of 742 newly-identified HIV-infected children enrolling into outpatient HIV care, 20.9% were identified by routine inpatient HIV testing. Compared to community-identified children, hospital-identified patients were younger (median 25.0 vs 53.5 months), with more severe disease (22.2% vs 7.8% WHO stage IV). Of 466 children with known outcomes, 15.0% died within the first year of HIV care; median time to death was 15.0 weeks for community-identified children vs 6.0 weeks for hospital-identified children. The strongest predictors of early mortality were severe malnutrition (hazard ratio, 4.3; 95% confidence interval, 2.2 – 8.3), moderate malnutrition (hazard ratio, 3.2; confidence interval, 1.6 – 6.6), age <12 months (hazard ratio, 3.2; 95% confidence interval, 1.4 – 7.2), age 12–24 months (hazard ratio, 2.5; 95%

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confidence interval, 1.1 – 5.7), and WHO stage IV (hazard ratio, 2.2; 95% confidence interval, 1.1 – 4.6). After controlling for other variables, hospital identification did not independently predict mortality.

Conclusions—Routine inpatient HIV testing identifies a subset of younger HIV-infected children with more severe, rapidly-progressing disease that traditional community-based testing modalities are currently missing.

Keywords

Africa; Antiretroviral therapy; HIV testing; Malawi; Pediatric HIV; Pediatric hospitals

INTRODUCTION

HIV continues to take a heavy toll on children in low-income countries, despite global strategies to scale up access to interventions preventing mother-to-child transmission (PMTCT) and pediatric antiretroviral therapy (ART).^{1,2} Children under the age of 15 account for an estimated 10% of the 34 million people living with HIV worldwide, and represent 14% of both new HIV infections and AIDS-related deaths.³ Progress has been made over the past 5 years. The number of children receiving ART increased 6-fold to an all-time high of 456,000 children in 2011, and PMTCT services now cover 48% of HIV-infected pregnant women globally. Together, these interventions contributed to greater than 20% reductions in both pediatric AIDS-related mortality and new pediatric HIV infections.³ However, a treatment gap remains. Less than one in four children eligible for ART are receiving therapy.³ The obstacles to scaling up pediatric HIV care in the context of stifling resource constraints have been well-documented.^{4,5} Along with prevention, among the most important strategies to circumvent these obstacles is identification of HIV-infected children early in life, in order to initiate ART, and thus reduce the infectious, metabolic, and neurocognitive complications of HIV and enhance survival.⁶

In Malawi, a southern African nation with an adult HIV prevalence of 11%, an estimated 120,000 children are currently living with HIV, more than half of whom are eligible for ART.¹ Located on the campus of Kamuzu Central Hospital (KCH) in Lilongwe, the Baylor College of Medicine-Abbott Fund Children's Clinical Centre of Excellence (COE) is the largest provider of pediatric ART in Malawi.⁷ The clinic initially offered comprehensive HIV care for children identified primarily through community-based client-initiated HIV testing and counseling (CITC) modalities and non-routine HIV testing in the hospital. But in 2008, KCH added routine pediatric inpatient provider-initiated HIV testing and counseling (PITC), which identified and linked an entirely new cohort of children into outpatient HIV care.^{8,9} However, it is not yet known whether identification of HIV-infected children by PITC, compared to traditional CITC modalities, has any impact on retention, mortality, or other outcomes of outpatient HIV care.

To answer these questions, we prospectively enrolled every newly-identified HIV-infected child referred for outpatient care at the COE over a 12-month period, and sought to determine whether children identified as HIV-infected by PITC differed at baseline from HIV-infected children identified by CITC. We then sought to determine factors, including

HIV testing strategy, that predict mortality within the first year of enrollment in outpatient HIV care.

METHODS

Study Setting

The Malawi Ministry of Health began scaling up access to ART for adults in 2004,¹⁰ but access to ART for children lagged prior to the establishment of the COE in 2006.⁷ The COE currently provides comprehensive HIV care to more than 5,000 HIV-infected children in central Malawi. Routine inpatient PITC is performed at KCH, which records more than 13,000 pediatric admissions per year, and has an inpatient pediatric HIV prevalence of 8.8%, as determined by routine inpatient HIV testing.⁹ Certified HIV counselors from community-based CITC programs or from the hospital test children using HIV antibody and/or DNA-PCR testing.^{8,9} HIV-exposed and infected children are then referred to the COE for registration. Notably, few community programs had access to DNA-PCR testing during the study period.¹¹

Study Design

This prospective study enrolled every newly-identified HIV-infected child that presented for an initial COE visit between January 1 and December 31, 2008. These patients were separated into two cohorts based on the location of their HIV test: within various CITC programs in the community versus PITC on the pediatric ward at KCH. At the initial COE visit, baseline clinical data were obtained for every child, including height, weight, World Health Organization (WHO) clinical stage, and ART eligibility status. Laboratory values included absolute CD4 for children 5 years and older, CD4 percent for children less than 5 years, and hemoglobin, whenever available. Any child that returned to the clinic 12 months later (range 11 – 13 months after the initial visit date) was considered to be an active patient in the program. Thus, one-year follow-up data were collected through January 31, 2009. Changes in WHO stage, anthropomorphic measurements, CD4 values, and hemoglobin levels were calculated for individual patients; thus, children who died, transferred out of the program, were lost-to-follow-up, or had either baseline or 1-year laboratory values missing were not included in these change-over-time calculations.

Definitions

PITC at KCH has been described in depth elsewhere.^{8,9} Briefly, mothers of all hospitalized children are offered an HIV test. Inpatient testing rates during the study period were 80–85%, due to lack of certified HIV counselors on the weekends; thus, this group is representative of all hospitalized children. All children <18 months of age whose mothers tested antibody-positive were offered a DNA PCR test, although not all children receiving a DNA PCR test received their results. Infants of mothers found to be antibody-negative were considered to be HIV-uninfected.^{8,9} Lost to follow-up was defined as any child enrolled in the program who failed to present for a clinic visit within a period of 11 to 13 months after program enrollment; children who failed to present during this two-month window but subsequently returned to care were still considered lost to follow-up in this study. In contrast, children transferred out are defined as newly-identified children whose outpatient

treatment was confirmed to be continued elsewhere; in most cases these children were deemed stable enough to be treated in facilities closer to their homes. ART eligibility is defined as any HIV-infected child under one year of age, any child under the age of 3 with <20% CD4%, any child between 3–5 years with <25% CD4%, any child older than five years with absolute CD4 cell count <200, and any child with WHO clinical stage III or IV disease. Of note, Malawi guidelines changed to include universal ART for all infants 12 months and under in April 2008, which corresponds to the time at which the first newly-identified infants in our study were initiated on ART; guidelines were subsequently revised to recommend universal ART for all children under age 24 months in July 2011, after the conclusion of this study. ART adherence is defined as the percent of clinic visits during the one-year follow-up period for which the caregivers brought the child's pills to the visit as instructed, and for which the number of remaining pills were determined by counting to be 95–105% what was expected.

Ethical Approval

The collection and use of this clinical data was approved by the Malawi National Health Sciences Research Committee and Baylor College of Medicine institutional review boards. De-identified data were extracted from electronic medical records and analyzed.

Statistical Methods

Weight-for-height z (WHZ), weight-for-age z (WAZ), and weight-for-height/length z (WHZ) scores were calculated for all children under the age of five years using the Child Growth Standards macro distributed by the WHO.¹² Subsequently, all children were assigned a wasting status; those with WHZ scores <−2 and <−3 were classified as moderately and severely wasted, respectively, whereas children 5 years and older were assigned a wasting status by manually plotting their height and weight on childhood growth charts published by the Malawi Ministry of Health.¹³

Normally-distributed data were reported using mean and standard deviation, and comparisons between two groups were made by independent-samples t test. Non-parametric continuous data were reported with median and interquartile range and compared by Mann-Whitney U test. Proportions were compared using Pearson's chi-square or Fisher's exact test. For categorical variables with multiple levels, a global chi-square test was performed; if this test indicated a significant difference somewhere among the data, individual post-hoc pair-wise comparisons were made using chi-square or exact tests, with Bonferroni's correction applied to adjust alpha for multiple comparisons. Only p values less than the corrected alpha were considered significant.

Cox proportional hazards analysis was used to identify predictors of mortality. Univariate hazard ratios (HR) with 95% confidence intervals (CI) were calculated. For multivariate analysis, laboratory values (CD4 percent, absolute CD4, and hemoglobin) were excluded *a priori*, given their large number of missing values and colinearity with other covariates, and a regression model was constructed using a two-step approach. First, site of HIV testing (PITC vs CITC) was entered into the equation because this was the main covariate of interest. Next, the remaining covariates were tested for entry with a forward stepwise

approach, with conditional entry based on the significance of the Wald statistic, and removal testing based on the change in log likelihood ratio. For multi-level categorical variables, a simple contrast method was used, in which each category of the predictor variable was compared to the reference category. The final multivariate model included age, nutritional status, WHO clinical stage, and testing modality. All calculations were performed using IBM SPSS Statistics 20 (IBM Corp., Chicago, IL).

RESULTS

We first sought to determine whether children identified as HIV-infected through routine inpatient HIV testing were clinically similar at baseline to the children identified by community-based testing. In a 12-month period, the two testing modalities identified a total of 742 HIV-infected children that subsequently enrolled into care at the COE, the majority (79.1%) of whom were identified by CITC (Table 1). The median age of PITC-identified children was 28.5 months younger than children identified through CITC. Children identified in the hospital had poorer nutritional status based on weight-for-age and weight-for-height criteria, and a 2.8-fold greater proportion of HIV-infected children identified by PITC had advanced WHO stage disease (7.8% of CITC vs 22.2% of PITC with WHO stage IV disease). There were no differences between the two groups with respect to gender, CD4+ cell levels, or hemoglobin levels.

After one year of outpatient HIV care, there were no differences between the two cohorts with respect to the proportion of children either lost to follow-up or transferred out of the program. However, the mortality rate for hospital-identified children, 15.5%, was double the 7.8% mortality rate for community-identified children (Table 1). Up to two causes of death were recorded in the hospital register by clinicians. Malnutrition was implicated in 21% of deaths, followed by sepsis and malaria in 16% and pneumonia in 13% of deaths (data not shown).

Among the barriers to scaling up routine pediatric hospital-based PITC is the perception that hospital-identified HIV-infected children are less likely to follow up and sustain good outcomes.^{8,14–16} To determine whether clinical outcomes of surviving HIV-infected children identified by CITC and PITC were similar, we examined medical records of the 396 HIV-infected children who remained in outpatient care at the COE one year after enrollment (Table 2). Overall, 80.3% of children were eligible for ART, although a higher proportion of ART-eligible children identified in the hospital, compared to those identified as HIV-infected in the community, were receiving ART one year after identification (91.4% vs 75.0%, $p = 0.005$). The median time from identification of HIV infection to initiation of ART for all children was just over 2 months, with a median duration of therapy of 9.7 months at the 12-month appointment.

After one year of enrollment in the COE outpatient care program, both cohorts showed profound improvements in both nutritional status and CD4 laboratory values. No differences were detected between the two groups with respect to ART adherence, nutritional status, WHO clinical stage, CD4 values, or hemoglobin levels. Thus, after one year of outpatient pediatric HIV care, children identified by routine inpatient HIV testing were less

distinguishable from children identified as HIV-infected by community-based testing than they were at baseline. Furthermore, although early mortality was higher among PITC-identified children, survivors demonstrated similar rates of adherence, follow-up, and response to treatment as CITC-identified children.

Finally, we sought to identify baseline clinical features among the 742 children with new HIV-infected diagnoses that could predict early mortality after enrollment in outpatient HIV care. Univariate survival analyses revealed that age less than 24 months, moderate or severe wasting, WHO stage IV, lower absolute CD4, lower hemoglobin, and identification by routine inpatient HIV testing as factors were associated with increased mortality within the first year of HIV care (Table 3). Multivariate logistic regression analysis revealed that moderate or severe wasting, WHO stage IV, and age less than 24 months were each independent predictors of early death. Although CITC-identified children who died had a longer median survival time than those in the PITC-identified cohort (15.0 vs 6.0 weeks, $p<0.001$; Figure 1), after controlling for age, nutritional status, and WHO stage, testing modality did not independently predict mortality at one year (Table 3). These data indicate that hospital-based PITC preferentially identifies the children at highest risk of early mortality, but that the site of testing does not by itself predict poor outcomes for HIV-infected children.

DISCUSSION

Routine hospital-based PITC has recently been shown to be a critical portal of entry into HIV care for children in regions facing high prevalence of HIV and resource limitations.^{8,9,14–18} However, outcomes of PITC-identified children are thought to be less favorable compared to children identified by traditional CITC systems. By prospectively enrolling newly-identified children from both CITC and PITC testing modalities and monitoring their outcomes over one year, we found that, despite PITC-identified children being younger, more malnourished, with more advanced HIV disease and a higher early mortality rate compared to CITC-identified HIV-infected children, there were no differences with respect to the default or lost-to-follow-up rate, in the time to ART initiation, or in ART adherence rates. Furthermore, clinical characteristics and one-year outcomes among the survivors were strikingly similar between the two cohorts. Thus, routine inpatient PITC identifies a subset of younger HIV-infected children with more severe, rapidly progressing disease that CITC-based testing is currently missing.

Our analyses reveal that that age <24 months, moderate or severe wasting, and WHO clinical stage IV, but not HIV testing strategy, independently predict mortality within the first year of HIV care. Two smaller studies from Lilongwe, Malawi revealed WHO stage IV, poor nutritional status, and severe immunodeficiency to be predictive of mortality at 3 and 6 months after ART initiation among 439 children,¹⁹ and age <18 months and WHO stage IV to be predictive of early death or defaulting among 258 children,²⁰ respectively. These earlier studies were undertaken prior to the recommendation of initiating universal ART for all HIV-infected Malawian infants and prior to the introduction of routine inpatient HIV testing at KCH in 2008. More recently, hemoglobin <9 g/dL was found to be the sole independent predictor of mortality among a cohort of 135 HIV-infected children in Nairobi,

Kenya, although WHZ <-2 and WHO clinical stage IV were both associated with increased mortality on univariate analysis.²¹ Among the strengths of our study, therefore, was a large sample size that allowed us to fully probe independent predictors of mortality in the context of newer national guidelines for ART initiation and novel pediatric HIV testing modalities in the hospital setting.

Identification of younger children with more advanced HIV disease provides evidence that inpatient PITC identifies high-risk children known as “fast progressors,” a poorly-understood biological phenomenon that appears to be related to a combination of host and viral factors.^{22–27} These younger, more severely ill children are critical targets for ART scale-up programs, but our data reveal that they are not being identified by traditional community-based testing approaches. When unidentified, many of these children likely die at home or in hospitals before their HIV status becomes known. Given the strong evidence that ART initiation very early in life dramatically reduces both mortality and HIV disease progression,²⁸ we recommend routine inpatient HIV testing as an integral adjunct to the identification of HIV-infected children, including those younger and at higher risk. This subpopulation is being missed by initial HIV testing modalities including immunization clinics and early infant diagnosis programs, and would likely benefit most from early identification and access to HIV care.

Children identified by either testing approach demonstrated dramatic improvements in CD4 laboratory values, hemoglobin levels, and nutritional status after one year of HIV care at the COE. Among the few differences between the two cohorts after one year was the proportion of ART-eligible children on therapy. Reasons for lower rates of ART initiation among community-identified children warrant further investigation, but may include our finding that a greater proportion of HIV-infected infants identified in the hospital met the relatively straightforward criteria for age-based ART initiation (47% of hospitalized ART-eligible children were eligible due to age <12 months), compared to the community-identified children (just 23% of ART-eligible were eligible due to age <12 months). For older children, more complicated WHO clinical staging or laboratory-based criteria, which are often not immediately available in resource-constrained settings, must be used to determine ART eligibility. Alternatively, clinicians might perceive ART initiation to be more urgently needed in the group with visibly more clinically-advanced (or faster-progressing) disease, despite equal ART eligibility by standard criteria. Other reasons for not starting ART may include the rigorous initiation criteria employed at the COE, which includes identification of two caregivers per child, both of whom need to complete multiple ART training sessions. Anecdotally, very few caregivers declined starting therapy. It should be noted that one-year outcomes were known for just 53% of children, primarily due to the large number of patients transferring to lower-acuity outpatient centers closer to their homes, and to our study’s strict definition of lost to follow-up (patients returning to clinic more than 4 weeks after a missed 12-month appointment were still considered lost to follow-up). Nonetheless, these data reinforce the finding that favorable outcomes can be achieved in pediatric HIV care programs, even among subgroups of HIV-infected children shown to be at the highest risk of dying.

Among the weaknesses of our study, laboratory values including CD4 and hemoglobin were not routinely available in this resource-constrained setting. Having baseline and one-year values for every child likely would have enhanced our ability to identify the highest-risk patients at their baseline clinic visit. However, these laboratory indicators are unavailable in many low-income regions;²⁹ thus, addition of these laboratory parameters would limit the utility of more complex predictive models in similar settings in Africa. Our study also revealed aspects of the HIV care program that could be improved. For example, the 11.1% rate of HIV-infected children lost to follow-up, similar to rates reported in multiple settings in sub-Saharan Africa,³⁰ was higher than attrition rates more recently reported in western³¹ and South Africa.³² Also, an unknown number of infants under the age of 18 months who had a DNA PCR test never received their test results; this delay in PCR test reporting likely disproportionately affected the younger hospital-identified cohort, and highlights the need to develop new point-of-care HIV testing strategies for infants in similar settings. Additionally, reducing the median duration, currently more than two months, between HIV care enrollment and ART initiation should be explored as another strategy to improve outcomes in all HIV-infected children. Given our finding that HIV-infected children identified in the hospital are at highest risk of early mortality, novel strategies to initiate ART earlier might explore the possibility, for example, of point-of-care HIV testing³³ coupled to inpatient ART initiation. Finally, future studies could examine characteristics of newly-identified HIV-infected children not presenting to outpatient care. We have shown previously that 67–78% of HIV-infected children identified at KCH subsequently enrolled in the COE clinic;⁹ however, these rates are unknown for the multiple community-based testing centers referring new patients to the COE. A thorough understanding of the reasons for not presenting for follow-up would strengthen this and other HIV care programs throughout Africa.

In summary, this study reveals that the community-based CITC strategies currently being utilized throughout sub-Saharan Africa are failing to identify a critical subset of younger HIV-infected children who are in urgent need of immediate access to HIV care including ART. Thus, HIV testing in the pediatric hospital will be an important component of comprehensive HIV testing programs in areas of high HIV prevalence, and, along with novel community-based approaches such as door-to-door household testing and integration of HIV testing with childhood immunization schedules,^{34,35} will likely play a central role in a successful scale-up of access to pediatric HIV care worldwide.

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FIGURE 1.

Kaplan-Meier survival estimates stratified by testing modality. *CITC*, community-based client-initiated HIV testing and counseling; *PITC*, routine pediatric inpatient provider-initiated HIV testing and counseling.

TABLE 1

Characteristics of HIV-Infected Children Enrolling in Outpatient Care (N = 742)

	CITC (n = 587)	PITC (n = 155)	P
Baseline Characteristics			
Age, mos, median (IQR)	53.5 (24.1 – 94.5)	25.0 (14.3 – 50.1)	<0.001
Sex, female (%)	302 (51.4)	76 (49.0)	0.593
WAZ score, Mean (SD) ¹	–2.12 (1.62)	–2.66 (1.82)	0.002
HAZ score, Mean (SD) ¹	–2.51 (1.73)	–2.83 (1.81)	0.089
WHZ score, mean (SD) ¹	–0.94 (1.67)	–1.55 (1.86)	0.001
Moderately/severely wasted, n/N (%)	93/583 (16.0)	51/153 (33.3)	<0.001
Severely wasted, n/N (%)	43/583 (7.4)	31/153 (20.3)	<0.001
WHO stage, n/N (%)			<0.001
I	167/562 (29.7)	35/144 (24.3)	NS
II	151/562 (26.9)	22/144 (15.3)	<0.0125
III	200/562 (35.6)	55/144 (38.2)	NS
IV	44/562 (7.8)	32/144 (22.2)	<0.0125
Absolute CD4 counts, mean (SD) ²	400.0 (352.0)	480.0 (428.0)	0.251
Percent CD4, mean (SD) ³	21.0 (9.8)	19.5 (8.6)	0.154
Hemoglobin g/dL, mean (SD) ⁴	9.9 (2.1)	9.7 (2.0)	0.361
Follow-Up			
One-year outcome, n (%)			0.018
Active patients	324 (55.2)	72 (46.5)	NS
Died	46 (7.8)	24 (15.5)	<0.0125
Transferred out	131 (22.3)	39 (25.2)	NS
Lost to follow-up	86 (14.7)	20 (12.9)	NS

¹ WAZ, HAZ, and WHZ scores presented for 328 CITC- and 125 PITC-identified patients. Additionally, all children with weight recorded at baseline were classified according to moderate/severe wasting (if over 5, Malawi Ministry of Health criteria were used).

² Absolute CD4 available for 262 CITC- and 29 PITC-identified children <5 years of age.

³ CD4 percent available for 285 CITC- and 109 PITC-identified children ≥ 5 years of age.

⁴ Hemoglobin available for 358 CITC- and 105 PITC-identified children.

CITC, community-based client-initiated HIV testing and counseling; IQR, interquartile range; PITC, routine pediatric inpatient provider-initiated HIV testing and counseling; SD, standard deviation; WHO, World Health Organization; WAZ, weight-for-age Z; HAZ, height-for-age Z; WHZ, weight-for-height Z.

TABLE 2

Profiles of HIV-Infected Children Remaining in Outpatient Care After One Year (N = 396)

	CITC (n = 324)	PITC (n = 72)	P
Number of outpatient visits, median (IQR)	17 (15 – 21)	18 (15 – 20)	0.960
Percent of visits ART Adherent ¹ , mean (SD)	66.2 (19.9)	66.8 (21.6)	0.866
WHO stage, n (%)			0.527
I	54 (16.7)	11 (15.3)	
II	93 (28.7)	16 (22.2)	
III	139 (42.9)	33 (45.8)	
IV	38 (11.7)	12 (16.7)	
Advancement of WHO stage, n (%)	78 (24.1)	16 (22.2)	0.738
ART eligible, n (%)	260 (80.2)	58 (80.6)	0.953
On ART, n/N (%) ²	195/260 (75.0)	53/58 (91.4)	0.005
Median time to ART initiation after enrollment, months (IQR)	2.4 (1.4 – 4.4)	2.4 (1.2 – 4.9)	0.419
Median time on ART, months (IQR)	9.5 (7.5 – 10.7)	10.0 (6.9 – 11.0)	0.972
Children on ART³	n = 195	n = 53	
WAZ score, mean (SD)	−1.20 (1.14)	−1.11 (1.51)	0.721
Change in WAZ, mean (SD)	+0.80 (1.42)	+1.16 (1.37)	0.199
HAZ score, mean (SD)	−2.48 (1.51)	−2.38 (1.96)	0.770
Change in HAZ, mean (SD)	−0.07 (1.44)	+0.20 (1.54)	0.375
WHZ score, mean (SD)	0.31 (1.14)	0.35 (1.32)	0.871
Change in WHZ, mean (SD)	+1.24 (1.69)	+1.45 (1.89)	0.541
Hemoglobin g/dL, mean (SD)	11.0 (2.4)	10.9 (1.6)	0.923
Change in hemoglobin g/dL, mean (SD)	+1.1 (2.6)	+0.9 (1.4)	0.739
Absolute CD4 counts, mean (SD)	579.0 (412.3)	648.5 (267.1)	0.516
Change in absolute CD4, mean (SD)	+317.6 (390.4)	+374.3 (223.0)	0.574
Percent CD4, mean (SD)	30.7 (9.0)	29.8 (9.8)	0.618
Change in percent CD4, mean (SD)	+11.7 (10.6)	+11.3 (10.2)	0.863
Children not on ART⁴	n = 129	n = 19	
WAZ score, mean (SD)	−1.05 (1.39)	−0.47 (1.39)	0.255
Change in WAZ, mean (SD)	+0.45 (1.24)	+0.69 (0.99)	0.571
HAZ score, mean (SD)	−2.26 (1.58)	−2.01 (1.60)	0.664
Change in HAZ, mean (SD)	−0.09 (1.30)	+0.40 (0.80)	0.271
WHZ score, mean (SD)	0.39 (1.13)	1.04 (1.03)	0.115
Change in WHZ, mean (SD)	+0.73 (1.61)	+0.82 (1.02)	0.875
Hemoglobin g/dL, mean (SD)	11.0 (1.8)	10.1 (1.7)	0.322
Change in hemoglobin g/dL, mean (SD)	+0.8 (1.9)	+0.0 (2.0)	0.394
Absolute CD4 counts, mean (SD)	574.6 (292.2)	735.9 (373.0)	0.146
Change in absolute CD4, mean (SD)	−62.1 (346.1)	+190.0 (349.4)	0.051
Percent CD4, mean (SD)	25.2 (8.9)	29.5 (9.5)	0.263

	CITC (n = 324)	PITC (n = 72)	P
Change in percent CD4, mean (SD)	+2.9 (8.6)	+4.0 (13.8)	0.780

¹ An adherent outpatient visit is defined as 1) pills brought and 2) between 95–105% of correct number of pills counted; adherence was assessed at each visit over the one-year follow-up period.

² ART regimens for community-identified children: 1 AZT-3TC-NVP, 5 d4T-3TC-EFV, 189 d4T-3TC-NVP; for hospital-identified children: 1 d4T-3TC-EFV, 52 d4T-3TC-NVP.

³ Children on ART: Z scores calculated for all 86 CITC- and 35 PITC-identified children under age five; hemoglobin data available for 71 CITC- and 23 PITC-identified children; absolute CD4 data available for 98 CITC- and 16 PITC-identified children over age five; CD4% data available for 78 CITC- and 35 PITC-identified children under age five.

⁴ Children not on ART: Z scores calculated for all 31 CITC- and 10 PITC-identified children under age five; hemoglobin data available for 35 CITC- and 5 PITC-identified children; absolute CD4 data available for 93 CITC- and 8 PITC-identified children over age five; CD4% data available for 80 CITC- and 8 PITC-identified children under age five.

ART, antiretroviral therapy; CITC, community-based client-initiated HIV testing and counseling; IQR, interquartile range; PITC, routine pediatric inpatient provider-initiated HIV testing and counseling; SD, standard deviation; WHO, World Health Organization; WAZ, weight-for-age Z; HAZ, height-for-age Z; WHZ, weight-for-height Z.

TABLE 3
Multivariate Cox Regression Analysis of Baseline Predictors of Early Mortality for HIV-Infected Children (N = 742)

Clinical Characteristics	N	Survival Status			Crude HR (95% CI)	P	Adjusted HR (95% CI)	P
		Died	Censored					
Age, months								
< 12	97	21 (21.6)	32		6.5 (3.1 – 13.5)	<0.001	3.1 (1.4 – 7.1)	0.007
12 – 23.9	123	23 (18.7)	48		6.1 (3.0 – 12.6)	<0.001	2.5 (1.1 – 5.7)	0.033
24 – 59.9	221	15 (6.8)	101		2.1 (1.0 – 4.6)	0.059	1.4 (0.6 – 3.1)	0.481
60	301	11 (3.7)	95		Reference		Reference	
Sex								
Male	364	39 (10.7)	138		1.4 (0.9 – 2.1)	0.198	–	–
Female	378	31 (8.2)	138		Reference		–	–
Nutritional status								
Normal/mild wasting	592	28 (4.7)	223		Reference		Reference	
Moderate wasting	70	13 (18.6)	23		4.5 (2.3 – 8.7)	<0.001	3.2 (1.6 – 6.6)	0.001
Severe wasting	74	27 (36.5)	28		10.6 (6.2 – 18.1)	<0.001	4.2 (2.2 – 8.2)	<0.001
WHO stage								
I	202	16 (7.9)	71		Reference		Reference	
II	173	2 (1.2)	58		0.1 (0.03 – 0.6)	0.008	0.2 (0.05 – 0.9)	0.039
III	255	24 (9.4)	94		1.2 (0.7 – 2.3)	0.496	1.0 (0.5 – 1.9)	0.947
IV	76	22 (28.9)	25		4.2 (2.2 – 8.0)	<0.001	2.2 (1.1 – 4.6)	0.034
Testing modality								
CITC	587	46 (7.8)	217		Reference		Reference	
PITC	155	24 (15.5)	59		2.0 (1.2 – 3.3)	0.005	1.1 (0.6 – 1.8)	0.805
Laboratory Indicators [/]								
Absolute CD4 count	291	11	85		0.996 (0.992 – 0.999)	0.024	–	–
Percent CD4	394	42	152		0.989 (0.956 – 1.022)	0.499	–	–
Hemoglobin g/dL	463	50	123		0.725 (0.639 – 0.822)	<0.001	–	–

[/] Due to large number of missing values and collinearity, laboratory indicators were left out of the multivariate model

CI, confidence interval; CITC, community-based client-initiated HIV testing and counseling; PITC, routine pediatric inpatient provider-initiated HIV testing and counseling; WHO, World Health Organization.