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High Prevalence of non-adherence to antiretroviral therapy among undisclosed HIV-infected children in Ghana

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Abstract

Adherence to antiretroviral therapy (ART) remains one of the greatest obstacles in pediatric HIV care. We sought to determine the prevalence of adherence to ART among undisclosed HIV-infected children and adolescents in Ghana. We analyzed baseline data from HIV-infected children and adolescents aged 7 to 18 years old enrolled in the SANKOFA Pediatric HIV disclosure intervention study in Ghana. Antiretroviral medication adherence was measured using caregiver 3-day recall; child 3-day recall; and pharmacy records for antiretroviral time-to-refill. Four hundred and twenty child-caregiver dyads were enrolled from January 2013 to June 2016. The median adherence (interquartile range), as measured by time-to-refill, was 93.2% (68.0% – 100.0%). However, only 47.5% of children had ≥95% adherence ("good adherence") using time-to-refill data. Children of caregivers who had received secondary or higher level of education versus no

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school (aOR, 2.90, 95% Confidence Interval, CI 1.29 to 6.56), p = 0.010) or elementary education only (aOR, 2.20, CI, 1.24 to 3.88, p = 0.007) were more likely to have “good adherence” (≥95%). In this cohort of children unaware of their HIV positive status, median ART adherence rate was sub-optimal (by World Health Organization definition) while 38% had poor adherence (<85%).

Keywords

Adherence; Sub-Saharan Africa; Antiretroviral therapy; Pediatrics

INTRODUCTION

The global burden of HIV-infected children remains significant, with sub-Saharan Africa being home to about 90% of HIV-infected children worldwide (World Health Organization, UNAIDS, & UNICEF, 2011). With expanded global access to antiretroviral therapy (ART), adherence to ART has become an issue of major global health concern (Joint United Nations Programme on HIV/AIDS, 2014). Poor adherence to ART is associated with treatment failure, evolution of HIV drug-resistant virus, and high prevalence of HIV-associated morbidity and mortality (Bangsberg et al., 2001; Bezabhe, Chalmers, Bereznicki, & Peterson, 2016; Parienti et al., 2004). Studies have shown that levels of adherence as high as 95% are necessary in order to maintain sustainable viral suppression, especially in ART regimens still in resource-limited settings (Parienti et al., 2004; D.L. Paterson et al., 2000). However, in many studies in resource-limited settings, adherence has been shown to be sub-optimal, even in areas where government-sponsored free ART clinics are available at the local level (Aragones, Sanchez, Campos, & Perez, 2011; Biressaw, Abegaz, Abebe, Taye, & Belay, 2013; Eticha & Berhane, 2014). Non-adherence to ART is of particular concern in HIV-infected children, who often require caregiver assistance in order to maintain adherence and to cultivate life-long adherence habits (Santer, Ring, Yardley L., Geraghty, & Wyke, 2014).

There are multiple reasons described as influencing adherence to ART, including disclosure of status (Cluver et al., 2015; Nichols, Steinmetz, & Paintsil, 2016), stigma (Muller, Bode, Myer, Stahl, & von Steinbuchel, 2011), child’s age (Ugwu & Eneh, 2013), and family support (Tiyou, Belachew, Alemseged, & Biadgilign, 2010). Levels of adherence and various factors affecting adherence must be elucidated within patient populations in order to maintain adherence habits necessary to cultivate a lifelong suppression of viremia. Efforts to understand current levels of adherence and barriers of adherence will be crucial in achieving viral suppression in accordance with 90–90-90 targets (Joint United Nations Programme on HIV/AIDS, 2014).

In Ghana, there are over 34,000 children living with HIV, accounting for about 10% of HIV-infected individuals in the country (Ghana AIDS Commission (GAC), 2014; Reynolds et al., 2015). Many of these children are not aware of their HIV-positive status; a recent study examining one of the pediatric HIV programs in Ghana revealed that only 21% of HIV-positive children from 8–14 years old knew their positive HIV status (Kallem, Renner, Ghebremichael, & Paintsil, 2011). The SANKOFA project is a site-randomized, controlled

pediatric HIV disclosure intervention trial in Ghana enrolling children and adolescents unaware of their HIV-positive status and their caregivers (Reynolds et al., 2015). In this study, we sought to elucidate the level of medication adherence among HIV-positive children who did not know their HIV status and determine factors predictive of adherence in this population.

METHODS

Study design and population

The details of the SANKOFA study design and study population have been published elsewhere (Catlin et al., 2015; Reynolds et al., 2015). In brief, the SANKOFA study is a site-randomized clinical trial that is testing a structured disclosure intervention for caregivers of HIV-infected children at two sites in Ghana (Reynolds et al., 2015). Patients enrolled at the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, were randomized to receive an adherence and disclosure specialist (ADDS) intervention plus normal care, while patients enrolled at the Korle-Bu Teaching Hospital (KBTH) in Accra, Ghana, received clinical standard of care only. Site randomization was used instead of patient randomization in order to avoid cross-contamination of the intervention and control arms. Eligible participants included patients 7–18 years old started on ART who did not know their HIV status at enrollment. The child’s knowledge about their status was determined by a pre-enrollment screening of medical records and interview with the child’s caregiver. Exclusion criteria include AIDS-defining illness, congenital disorders and illnesses such as sickle cell disease or diabetes requiring regular clinic or hospital care. This analysis included patients enrolled from January 2013—June 2016. The study protocol was reviewed and approved by the Institutional Review Boards of the University of Ghana Medical School, Komfo Anokye Teaching Hospital, and Yale University. Written informed consent and assent were obtained from the caregivers and children, respectively.

Study Measurements

Demographic data collected at enrollment included: age and gender of caregiver and child, household income, employment status, distance from the hospital, education level (caregiver and child), marriage status of the caregiver, HIV status of the caregiver, and duration of the child’s ART therapy.

Child’s medication adherence: Children’s adherence to ART was assessed using three measures: (1) caregiver three-day recall using a modified version of the self-report questionnaire developed by the Adult AIDS Clinical Trials Group (AACTG) (Chesney et al., 2000; Duong et al., 2001); (2) child three-day recall; and (3) pharmacy-based time-to-refill of ART (Ernesto et al., 2012; Grossberg, Zhang, & R., 2004). Self-reported adherence in a three-day recall period was analyzed as either “100% adherence” (no missed doses) in a three-day period or as “<100% adherence” (at least one missed dose) during that three-day period. While older patients may not have been directly supervised by caregivers in taking their medication, caregivers attended clinic visits and obtained pharmacy refills with their children; thus, it is reasonable to assume that caregivers were integrally involved in obtaining and administering medications for most patients considering that patients were

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unaware of their status. In order to determine the pharmacy-based time-to-refill measure, pharmacy records were retrospectively examined for the refill period closest to the time of study entry to determine dates of most recent refill and dosages of ART administered for the refill period at study entry. Patients were typically given thirty days of medication in one refill period, although some patients received greater than thirty days of medication at the time of refill prior to study enrollment. Adherence was calculated by using the number of pills administered in a refill period, corrected by pill count when available, to determine the estimated number of doses taken in a refill period. This was then divided by the number of expected doses taken during that period of time, and the results multiplied by 100 to determine the percentage of expected doses taken.

CD4 cell count and HIV viral load measurements: CD4 absolute count and percentage were quantified by a dual-platform flow cytometry technology using a FACSCount system (Becton-Dickinson, Franklin Lakes, NJ, USA) at the clinical laboratories at KATH and KBTH according to manufacturer's instructions. The HIV RNA viral load testing was performed using the COBAS ® AMPLICOR Monitor test (Roche Diagnostic Systems, Branchburg, NJ, USA). The limit of HIV-1 RNA detection was 20 copies/mL. The laboratories are certified by the South African Public Health Reference Laboratory and participate in an external quality assurance testing program by the South African Public Health Reference Laboratory. Viral load and CD4 counts were accepted within six months of entry into the study.

Definitions

The WHO provides a guide for estimating adherence: adherence is classified as either "good adherence" (i.e., ≥ 95%), "fair adherence" (i.e., 85%−94%), and "poor adherence" (i.e., <85%) (World Health Organization, 2010).

Statistical Analysis

Baseline demographic variables ART adherence, CD4 count, CD4 percentage and viral load data for the caregiver-child dyads were summarized using descriptive statistics. Means and medians (with Interquartile range, IQR) were calculated for these factors as appropriate. Comparisons between study arms for these factors was done using parametric tests (t-tests) for normally distributed variables and non-parametric techniques (Wilcoxon rank-sum tests) for variables with non-normal distributions. For categorical variables, numbers and percentages are provided, with chi-square or Fisher's exact test used for comparisons, as indicated. The association between ART adherence and demographic characteristics were assessed using univariate and multivariable logistic regression. Missing data were assumed to be missing at random (MAR). All analyses and reports were generated using SAS v9.3, SAS Inc.

RESULTS

Characteristics of child-caregiver dyads

We enrolled 440 child-caregiver dyads from January 2013 to June 2016 at the two study sites: KATH (n=2240) and KBTH (n=206). Since this was a site-randomized study to avoid

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cross-contamination of the intervention and control arms, all patients at KATH were enrolled with the intention to receive disclosure and adherence intervention, while those at KBTH received usual care. Table 1 illustrates the demographic and social characteristics of the children. About 52% of the children were male. The mean age of the children was 9.8± 2.3 years. Over 95% of children at both sites were in school. The predominant mode of HIV infection was mother-to-child transmission (MTCT) (83%). Children in the study had been diagnosed for a median (IQR) of 4.7 (2–6.8) years before study entry and had been on ART for a median (IQR) of 3.5 (1.07–5.7) years before enrollment. At the time of HIV diagnosis, 14%, 30%, 33.4%, and 11% of the children had WHO clinical stage 1, 2, 3, and 4, respectively. The median (IQR) CD4 count was 826 (509–1179) cells/mL, while a total of 20 children had CD4 counts <100 cells/mL at time of study entry. Of the 223 children who had viral loads available and who had been on ART for >3 months, 82 (18.4%) had viral loads >1000 copies/mL. Viral loads (n=143) and CD4 counts (n=62) were unavailable at entry for some patients due to reagent shortages and frequent breakdown of instruments during the course of study enrollment. About 59% of children were cared for by an HIV-infected caregiver; 78% of them received help from their caregivers in taking their ART medications. Though there were some significant demographic differences, baseline data regarding adherence were analyzed in aggregate rather than by comparing study sites.

Table 2 illustrates the demographic and social characteristics of the caregivers. The mean (SD) age of the caregivers was 42± 10.4 years; 80% were female. Although 83% of caregivers reported having received some form of formal education, only 29% of them had received a secondary or higher level of education. Although the majority of caregivers were employed (86%), they were mostly in the low socioeconomic bracket with household monthly income ≤ 300 GHC (the equivalent of ≤ US$80).

Prevalence of adherence and performance of various adherence measurements

ART adherence as measured by time-to-refill from pharmacy records was available for 401 of 440 dyads at baseline (Table 3). The median (IQR) adherence as measured by time-to-refill was 93.2% (68.0% – 100.0%). Of the 401 dyads, 199 (49.6%) had pill count data available. Those without pill count available at refill had adherence estimated by dividing the number of doses administered in the preceding refill period by the number of doses the patient had been expected to take in the dates between refill. Those with pill counts available had their number of doses administered adjusted to reflect their leftover pills. The median (IQR) adherence for those with pill count was 97.7% (85.2% – 100.0%), while median (IQR) adherence for those without pill count was 81.0% (48.0% – 100.0%). There was a significant difference in adherence between those with pill count available and those without (p<0.001). As per WHO categorization of adherence (World Health Organization, 2010), a total of 190 patients (47.5%) achieved ≥95% adherence (“good adherence”), while 58 (14.5%) had 85%−95% adherence (“fair adherence”) and 152 (38.0%) had <85% adherence (“poor adherence”).

Adherence was also assessed using child and caregiver three-day recall (Table 4). A total of 389 responses (88.4%) were available from children and 311 available from caregivers (70.7%). A total of 58 (14.9%) children who responded reported missing at least one dose in

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the past three days (<100% adherence), while a total of 47 (15.1%) caregivers who responded reported that their child had missed at least one dose in the past three days. The association between caregiver-reported adherence and adherence as determined by pharmacy record was statistically significant. There was no association between missed doses as reported by child recall and levels of adherence as determined by pharmacy record (Table 4).

Child and caregiver demographic characteristics associated with ≥95% adherence

A multivariable logistic regression was performed to determine predictors of ≥95% adherence using pharmacy record data (Tables 5 and 6). Only children (n=283) who had information available for all variables examined and had been on ART treatment for at least 3 months before enrollment were included in the regression model. Neither viral load nor CD4 count were included in the regression model due to a high number of missing values from entry due to frequent machine breakdowns and reagent shortages during enrollment. In addition, many patients had viral loads drawn within one to six months of medication initiation. Thus, viral load would not accurately reflect adherence in these patients, as they may not yet have achieved viral suppression even with ideal adherence. In the model that adjusted for children's demographics (Table 5), child reported help with medications from a biological parent (aOR, 0.48, 95% CI, 0.24 to 0.96, p = 0.04) versus those who reported no help with medications was also associated with <95% adherence. Child's age approached, but did not reach, statistical significance in predicting <95% adherence (aOR, 0.91, 95% CI, 0.81 to 1.02, p = 0.09).

A similar multivariable logistic model was run for caregiver demographics (n=303) (Table 6). In this analysis, children of caregivers who had received secondary or higher level of education versus no school (aOR, 2.89, 95% CI, 1.29 to 6.50, p = 0.01) or elementary education only (aOR, 2.21, 95% CI, 1.26 to 3.87, p = 0.006) had significantly good adherence (≥95%), while those who lived closer to the hospital (aOR, 0.49, 95% CI, 0.30 to 0.80, p = 0.004) had significantly lower levels of adherence. HIV-positive status of caregivers approached statistical significance for <95% adherence in the adjusted model (aOR, 0.61, 95% CI, 0.35 to 1.04, p = 0.07), but nonetheless did not reach statistical significance.

Discussion

We assessed the baseline levels of adherence using various measures among HIV-infected children and adolescents in Ghana who are not aware of their HIV status enrolled in the ongoing SANKOFA Pediatric HIV disclosure intervention trial. Median adherence (93%) by the pharmacy-based time-to-refill measure in this cohort of children and adolescents was fair, but only 48% of study participants achieved ≥95% adherence at study entry, while 38% had poor adherence (<85% adherence). Adherence to ART remains one of the most profound challenges to combating the HIV epidemic. In children and adolescents, development of adherence habits becomes even more crucial, as these must be developed to last a lifetime in order to achieve positive health outcomes. Our finding of sub-optimal baseline adherence among our study population is consistent with a study conducted by Biressaw et al. in Ethiopia (Biressaw et al., 2013) that reported that only 34.8% of patients

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were ≥95% adherent by unannounced home-based pill count. Interestingly, in our study, the group with available pill count data had higher median adherence (97.7%) than those without pill count available (81.0%). This may be explained by the fact that pill count allows for correction for the number of pills left over from a previous refill period in adherence calculation, thus providing a more precise measure of adherence.

Caregiver and child three-day adherence recall, a rapid screening method that has been used as a measure of adherence in other studies (Cluver et al., 2015; Nabukeera-Barungi, Kalyesubula, Kekitiinwa, Byakika-Tusiime, & Musoke, 2007), showed low adherence, with 14.9% of children reporting missing a dose in the preceding three-day window and 15.11% of caregiver reporting their child missing a dose in the preceding three days, albeit with a number of missing results (Table 4). These reported adherence levels are very similar to findings in other studies using caregiver or child recall to estimate adherence in sub-Saharan Africa (Biadgilign, Deribew, Amberbir, & Deribe, 2008; Nabukeera-Barungi et al., 2007; Turissini et al., 2013). However, adherence measured by three-day recall did not correlate well with adherence based on time-to-refill method (Table 4), a finding corroborated by other studies (Biressaw et al., 2013; Haberer et al., 2011).

The significance of optimal adherence to ART is universally recognized; however, there is no consensus on how to measure adherence. There are several measures of adherence, from self-reporting to pharmacy record-based calculations to sophisticated microelectronic monitors that record bottle openings and reconstruct complex pill-taking patterns (Bisson et al., 2008; Harries et al., 2004; Miller & Hays, 2000; Muller, Bode, Myer, Roux, & von Steinbuchel, 2008; Muller et al., 2011; Wendel et al., 2001). Our findings and that of other studies suggest that quick-screening measures relying on patient recall may not be sensitive in determining adherence in children, and thus should be used in conjunction with pharmacy record-based or electronic methods to adequately assess adherence, especially in settings where viral load measurement may not be available.

Several demographic factors were found to be significantly associated with ≥95% adherence on multivariable logistic regression. Higher level of caregiver education was associated with ≥95% adherence. Counterintuitively, we found that child self-reported help with medications and living closer distance to the hospital were indicative of lower adherence. However, this could be explained by the fact that the child self-reported help with medications in a structured entry interview, and thus different children may have interpreted “help” differently; some may have considered help to involve the “helper” giving the medication directly to the child each day, while others may have considered “help” to mean verbal reminders to take medications. There may also be greater stigma associated with an HIV-positive caregiver providing medications to their child, with the parent perhaps fearful of the child discovering the HIV positive status of either the child or the caregiver. The clinic distance conundrum could be explained by considering that those living farther away might be more likely to regularly keep clinic appointments and refill dates knowing they will have to travel some distance to do so. However, these variables provide questions for further exploration.

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Our study has several limitations. First, challenges with pharmacy staffing led to a difficulty obtaining pill count for many patients, leading to the use of less accurate (though previously validated) (Ernesto et al., 2012; Grossberg et al., 2004) pharmacy record-based time-to-refill to calculate adherence for about half of the patients. Because of the uneven split between those with pill counts available and those without, comparison between the sites was not possible. Second, this analysis uses data from one point in time and thus may not adequately represent ART adherence habits over time. ART adherence may vary for each patient over a longer time period depending on extenuating life circumstances. Third, there were missing values for caregiver-reported adherence, as intervention specialist interviewers had difficulties ascertaining medication cards from caregivers at time of entry interview. These cards were used to ask about specific medications and dosages for the three-day recall method. Fourth, laboratory equipment breakdowns and reagent shortages led to missing viral load and CD4 mesuarements; therefore, we did not have data on viral load and CD4 counts at entry for all the study participants to validate findings from self-report. While 36% of patients with viral load data available on ART >3 months had unsuppressed viremia (>1,000 copies/mL), the large number of missing lab results made correlation between viral load data and other adherence measures challenging. While some laboratory results were missing at random due to reagent shortages and machine breakdown, some data were missing when parents chose not to have labs drawn for their child. Thus, it is possible that “less” or “more” adherent dyads would have been more likely to skip laboratory testing. Viral loads may also not directly correlate with cross-sectional adherence measures, as changes in adherence may occur at any point in time. A patient with suppressed viral load and previously good adherence but with poor adherence in the month of study entry may be at risk of breakthrough viremia if these poor adherence habits continue.

Adherence precedes efficacy of ART and durability of sustained viral suppression (Harries et al., 2004; D. L. Paterson et al., 2000). In our study, there were a large number of patients on treatment for greater than three months who had not achieved viral suppression (Table 1) and an equally concerning portion of patients (38%) who had <85% adherence by pharmacy record at the period of study entry. While regular viral load monitoring would be the ideal measurement of treatment success, these laboratory measurements are not always available in resource-limited settings. Therefore, the measures of adherence used in this study may be helpful to supplement identifying patients at risk for breakthrough viremia. Adherence screening tools in this study revealed unacceptably low levels of adherence in children unaware of their HIV-positive status receiving ART treatment in Ghana.

Conclusion

Adherence to ART was sub-optimal (as defined by WHO guidelines) in this cohort of HIV-positive children who did not know their HIV status at time of enrollment to the SANKOFA study. It is essential for providers to utilize pharmacy, self-report and laboratory-based screening methods in order to identify patients that may be in need of greater adherence counseling to achieve the global health goals of lifelong viral suppression in the pediatric population.

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Table 1:

Children's demographic and HIV disease characteristics

	SANKOFA Study Site			
	KATH (N = 240)	***KBTH (N = 206)***	***Total (N =446)***	***P Value***
Gender				
Female	124 (51.67%)	92 (44.66%)	216 (48.43%)	0.14
Male	116 (48.33%)	114 (55.34%)	230 (51.57%)	
Age[a]				
Mean (SD)	10.30 (2.57)	9.35 (1.81)	9.83 (2.27)	<0.001 ***
Median (IQR)	10 (8–12)	9 (8–11)	9(8–11)	
School[b]				
Yes	222 (92.50%)	205 (99.51%)	427 (95.74%)	0.22
No	5 (2.08%)	1 (0.49%)	6 (1.35%)	
Patient refused to answer	1 (0.42%)	0 (0.00%)	1 (0.22%)	
Missing	12 (5.00%)	0 (0.00%)	12 (2.69%)	
HIV Transmission Mode				
MTCT	189 (78.75%)	183 (88.83%)	372 (83.41%)	0.08
Other	7 (2.92%)	15 (7.28%)	22 (4.63%)	
Missing	44 (18.33%)	8 (3.88%)	52 (11.66%)	
Duration of HIV(days)				
Mean (SD)	1667.19(1112.44)	1701.33(961.41)	1684.59(1040.80	0.74
Median (IQR)	1760(686–253)	1856(874–2462)	1831(793–2499)	
Duration of ART treatment(days)				
Mean (SD)	1192.62 (1013.8)	1395.81 (890.74)	1295.77 (957.13)	0.035 *
Median (IQR)	1204 (119–016)	1330 (686–2135)	1266 (392–2075)	
CD4 count				
Mean (SD)	790.31 (555.71)	974.08 (505.02)	880.76 (538.59)	<0.001 ***
Median (IQR)	725 (361–1091)	928 (652–1278)	826 (509–1179)	
Missing (not Missing)	45 (195)	189 (17)	62 (384)	
CD4 count level				
≤ 100 cells/ml	11 (4.58%)	9 (4.37%)	20 (4.48%)	0.70
> 100 cells/ml	184 (76.67%)	180 (87.38%)	364 (81.61%)	
Missing	45 (18.75%)	17 (08.25%)	62 (13.90%)	
CD4%				
Mean (SD)	24.17 (12.89)	29.26 (12.06)	26.69 (12.73)	<0.001 ***
Median (Range)	25 (14–35)	31 (21–38)	28 (18–6)	
Missing (not Missing)	55 (185)	24 (182)	79 (367)	
HIV Viral Load (copies/ml)[a]				
Median (IQR)	1872 (0 – 6886)	107 (0 – 8380)	255 (0 – 34602)	0.73

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	SANKOFA Study Site			
	KATH (N = 240)	*KBTH (N = 206)*	*Total (N =446)*	*P Value*
Missing (not Missing)	83 (157)	60 (146)	143 (303)	
HIV viral Load level				
≤ 1000 copies/ml	76 (31.67%)	96 (46.60%)	172 (38.57%)	<0.002 [**]
> 1000 copies/ml	81 (33.75%)	50 (24.27%)	131 (29.37%)	
Missing	83 (34.58%)	60 (29.13%)	143 (32.06%)	
HIV Viral Load level (>3 months on ART)				
≤ 1000 copies/ml	52 (21.67%)	89 (43.20%)	141 (31.61%)	0.037 [*]
> 1000 copies/ml	42 (17.50%)	40 (19.42%)	82 (18.39%)	
Missing	146 (60.83%)	77 (37.38%)	223 (50.00%)	
WHO Stagingat time of Diagnosis				
Stage 1	(12.50%)	33 (16.02%)	63 (14.13%)	0.06
Stage 2	76 (31.67%)	58 (28.16%)	134 (30.04%)	
Stage 3	68 (28.33%)	81 (39.32%)	149 (33.41%)	
Stage 4	18 (07.50%)	32 (15.53%)	50 (11.21%)	
Missing	48 (20.00%)	2 (0.97%)	50 (11.21%)	
HIV+caregiver				
Yes	141 (58.75%)	124 (60.19%)	265 (59.42%)	0.92
No or Unsure	94 (39.17%)	81 (39.32%)	175 (39.24%)	
Missing	5 (2.08%)	1 (0.49%)	6 (1.35%)	
Does anyone help you take your medicine?				
Yes	184 (76.67%)	163 (79.13%)	347 (77.80%)	0.13
No	33 (13.75%)	43 (20.87%)	76 (17.04%)	
Missing	23 (9.58%)	0 (0.00%)	23 (5.16%)	
Who helps you with your medicine most of the time? [b]				
Biological parent (Mother/Father)	128 (53.33%)	129 (62.62%)	257 (57.62%)	0.08
Family (Grandparent/Aunt/Uncle)	36 (15.00%)	20 (9.71%)	56 (12.56%)	
Other family member	15 (6.25%)	8 (3.88%)	23 (5.16%)	
Other	4 (1.67%)	1 (0.49%)	5 (1.12%)	
Missing	57 (23.75%)	48 (23.30%)	105 (23.54%)	

Footnotes:

VL level indicates VL at study entry regardless of ART initiation date, while VL level >3 months on ART indicates VL measured more than 3 months after ART initiation date. KATH, Komfo Anokye Teaching Hospital, Kumasi, Ghana; KBTH, Korle-Bu Teaching Hospital, Accra, Ghana; MTCT, mother-to-child-transmission; ART, antiretroviral therapy; WHO, World Health Organization

[a] non-equal variances, Satterthwaite method is applied to calculate adjusted DF

[b] sparse table, Fisher Exact test for p value

[*] P value less than 0.05

[**] P value less than 0.01

*** P value less than 0.001

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Table 2:

Caregivers' demographic characteristics

	SANKOFA Study Site			
	KATH (N = 240)	*KBTH (N = 206)*	*Total (N = 440)*	*P Value*
Age				
Mean (SD)	42.81 (10.96)	41.32 (9.68)	42.12 (10.41)	0.13
Median (IQR)	42 (36–48)	10 (35–45)	41 (35–47)	
MaritalStatus				
Single	32 (13.33%)	30 (14.56%)	62 (13.90%)	0.25
Married	127 (52.92%)	123 (59.71%)	250 (56.05%)	
Divorced or separated	32 (13.33%)	25 (12.1%)	57 (12.78%)	
Widowed	49 (20.42%)	28 (13.59%)	77 (17.26%)	
Gender				
Female	203 (84.58%)	161 (78.16%)	364 (81.61%)	0.08
Male	37 (15.42%)	45 (21.84%)	82 (18.39%)	
Education[a]				
Elementary Education	162 (67.50%)	79 (38.35%)	241 (54.04%)	<0.001***
Secondary & Post-secondary Education	36 (15.00%)	93 (45.15%)	129 (28.92%)	
Religious schooling only	3 (1.25%)	1 (0.49%)	4 (0.90%)	
No School	39 (16.25%)	33 (16.02%)	72(16.14%)	
Employment Status[a]				
Unemployed	34 (14.17%)	27 (13.11%)	61 (13.68%)	0.30
Self-employed	188 (78.33%)	155 (75.24%)	343 (76.91%)	
Private or Government sector employment	17 (7.08%)	23 (11.17%)	40 (8.97%)	
Patient refused to answer	0 (0.00%)	1 (0.49%)	1 (0.22%)	
Missing	1 (0.42%)	0 (0.00%)	1 (0.22%)	
Monthly House hold Income[a]				
Less than 50 GHC[ǂ]	41 (17.08%)	4 (1.94%)	45 (10.09%)	<0.001***
50–300 GHC	155 (64.58%)	117 (56.80%)	272 (60.99%)	
Greater than 300 GHC	42 (17.50%)	79 (38.35%)	121 (27.13%)	
Patient refused to answer	0 (0.00%)	4 (1.94%)	4 (0.90%)	
Missing	2 (0.83%)	2 (0.97%)	(0.90%)	
Family members/other people in home(Child)[b]				
Median (IQR)	3 (2–5)	3 (2–3)	3 (2–4)	<0.001***
Family members/other people in home(Adult)[b]				
Median (IQR)	3 (2–5)	2 (2–3)	2 (2–4)	<0.001***
Number of living children[b]				

	SANKOFA Study Site			
	KATH (N = 240)	***KBTH (N = 206)***	***Total (N = 440)***	***P Value***
Median (IQR)	3 (2-)	3 (2–3)	3 (2–4)	0.35 *
Distance from Clinic				
0–20 kilometers	171 (71.25%)	110 (53.40%)	281 (63.00%)	<0.001 ***
More than 20 kilometers	62 (27.92%)	96 (46.60%)	163 (36.55%)	
Missing	2 (0.83%)	0 (0.00%)	2 (0.45%)	
Receiving own car eat:[a]				
Clinic/Hospital	235 (97.92%)	203 (98.54%)	438 (98.21%)	1.00
Clinic/Hospital and traditional/homeopathic healer	2 (0.83%)	1 (0.49%)	3 (0.67%)	
Other	2 (0.83%)	1 (0.49%)	2 (0.45%)	
Missing	1 (0.42%)	1 (0.49%)	2 (0.45%)	
Frequency of visits to traditional/homeopathic healer				
One or more times a year	35 (14.58%)	33 (16.02%)	68 (15.25%)	0.68
Once or never in last 5 years	202 (84.17%)	171 (83.01%)	373 (83.63%)	
Missing	3 (1.25%)	2 (0.97%)	5 (1.12%)	
Frequency of visits to clinic/hospital[a]				
One or more times a year	156 (65.00%)	168 (81.55%)	324 (72.65%)	<0.001 ***
Once or never in last 5 years	80 (33.33%)	38 (18.45%)	118 (26.46%)	
Other	1 (0.42%)	0 (0.00%)	1 (0.22%)	
Missing	3 (1.25%)	0 (0.00%)	(0.67%)	

Footnotes:

KATH, Komfo Anokye Teaching Hospital, Kumasi, Ghana; KBTH, Korle-Bu Teaching Hospital, Accra, Ghana

[a] sparse table, Fisher Exact test for p value

[b] non-equal variances, Satterthwaite method is applied to calculate adjusted DF

[ǂ] Ghana Cedis (GHS): 1 GHS = 0.31 USD

[*] P value less than 0.05

[**] P value less than 0.01

[***] P value less than 0.001

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Table 3:

Medication adherence by pharmacy records of time-to-refill for the two sites.

	Baseline ART Adherence type		
	Baseline ART Adherence: Pill Count (N = 199)	***Baseline ART Adherence: No Pill Count (N = 202)***	***Total (N = 401)***
Baseline ART adherence measure			
Median (IQR)	97.7% (85.2–100.0%)	81.0% (48.0–100.0%)	93.2% (68.0–100.0%)
Adherence categorization			
Poor Adherence (<85%)	48 (24.12%)	104 (51.49%)	152 (37.91%)
Fair Adherence (85% - 95%)	37 (18.59%)	21 (10.40%)	58 (14.46%)
Good Adherence (≥95%)	114 (57.29%)	76 (37.62%)	190 (47.38%)
Missing	0 (0.00%)	1 (0.50%)	1 (0.25%)

Footnotes:

ART, antiretroviral therapy

Patients with pill count available to supplement pharmacy refill records were included in the "Pill Count" column, while those without pill count available at enrollment were included in the "No Pill Count" column.

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Table 4:

Adherence by 3-day recall by child and caregiver is stratified into yes and no compared to adherence determined by pharmacy record.

	Adherence by Pharmacy Record			
	Not Good Adherence (<95%) (N = >210)	***Good Adherence (≥ 95%) (N = 190)***	***Total (N = 400)***	***P Value***
Baseline child-reported ART adherence: 3-day recall				
Yes (N=331)	177 (53.47%)	154 (46.53%)	331 (85.09%)	0.62
No (N = 58)	29 (50.00%)	29 (50.00%)	58 (14.91%)	
Baseline caregiver-reported ART adherence: 3-day recall				
Yes (N = 264)	112 (42.42%)	152 (57.58%)	264 (84.89%)	<0.001 ***
No (N = 47)	36 (76.60%)	11 (23.40%)	47 (15.11%)	

Footnote:

* P value less than 0.05

** P value less than 0.01

*** P value less than 0.001

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Table 5:

Multivariable logistic regression examining the association of child demographic characteristics with ≥95% adherence.

	Unadjusted model			Adjusted (multivariable model)		
Child Demographics	**Odds Ratio (95% CI)**	**SE**	**P value**	**Odds Ratio (95% CI)**	**SE**	**P value**
Age of child						
Increase by 1 year	0.95 (0.86, 1.05)	0.05	0.33	0.91 (0.81, 1.02)	0.06	0.09
Duration of HIV diagnosis (years)						
Increase by 1 year	1.03 (0.93, 1.13)	0.05	0.57	1.05 (0.88, 1.24)	0.09	0.60
Duration of ART treatment (years)						
Increase by 1 year	1.05 (0.95, 1.17)	0.05	0.30	0.92 (0.92, 1.12)	0.09	0.38
Duration of ART treatment						
> 6 months vs. ≤ 6 months	0.72 (0.21, 2.41)	0.62	0.59	0.77 (0.18, 3.24)	0.73	0.72
Gender						
Female vs. Male	0.87 (0.54, 1.39)	0.24	0.56	0.85 (0.52, 1.39)	0.25	0.52
HIV Transmission Mode						
MTC vs. Other	0.46 (0.16, 1.27)	0.52	0.13	0.49 (0.16, 1.47)	0.56	0.20
School attendance						
Yes vs. No	2.66 (0.27, 25.84)	1.16	0.40	3.30 (0.29, 38.04)	1.25	0.34
Help with medication						
Mother/Father vs. No help	0.57 (0.30, 1.09)	0.33	0.09	0.48 (0.24, 0.97)	0.36	0.04*
Grandparent/Aunt/Uncle vs. No help	0.54 (0.23, 1.30)	0.44	0.17	0.50 (0.20, 1.21)	0.46	0.12
Other help vs. No help	0.58 (0.20, 1.67)	0.54	0.32	0.47 (0.16, 1.38)	0.55	0.17
Mother/Father vs. Grandparent/Aunt/Uncle	1.05 (0.51, 2.14)	0.36	0.90	0.97 (0.47, 2.02)	0.37	0.94
Mother/Father vs. Other help	0.98 (0.39, 2.47)	0.47	0.96	1.03 (0.40, 2.70)	0.49	0.94
Grandparent/Aunt/Uncle vs. Other help	0.93 (0.13, 2.78)	0.56	0.90	1.06 (0.35, 3.28)	0.57	0.91

Footnote:

*p<0.05 is considered statistically significant, SE = Standard Error

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Table 6:

Multivariable logistic regression examining the association of caregiver demographic characteristics with ≥95% adherence.

	Unadjusted model			Adjusted (multivariable model)		
Caregiver Demographics	**Odds Ratio (95% CI)**	**SE**	**P value**	**Odds Ratio (95% CI)**	**SE**	**P value**
Age						
Increase by 1 year	0.99 (0.97, 1.01)	0.01	0.36	0.99 (0.96, 1.02)	0.01	0.43
Gender						
Female vs. Male	0.77 (0.44, 1.36)	0.29	0.37	1.13 (0.59, 2.14)	0.33	0.71
HIVStatus						
Yes vs. No or unsure	0.67 (0.42, 1.06)	0.24	0.09	0.61 (0.35, 1.04)	0.28	0.07
Education						
Elementary education vs. No school	1.13 (0.57, 2.26)	0.35	0.72	1.31 (0.64, 2.70)	0.37	0.46
Secondary & post-secondary education vs. No school	2.68 (1.27, 5.65)	0.38	0.009	2.89 (1.29, 6.50)	0.41	0.010 *
Secondary & post-secondary education vs. Elementary education	2.36 (1.40, 3.98)	0.27	0.001**	2.21 (1.26, 3.87)	0.29	0.006 *
Monthly House hold Income						
Greater than 300 GHC vs. Less than 50 GHC	2.14 (0.83, 5.56)	0.49	0.12	1.49 (0.55, 4.06)	0.51	0.44
50–300 GHC vs. Less than 50 GHC	1.83 (0.74, 4.54)	0.49	0.19	1.67(0.65, 4.26)	0.48	0.29
Greater than 300 GHC vs. 50-300 GHC	1.17 (0.70, 1.94)	0.26	0.55	0.89 (0.52, 1.54)	0.28	0.68
Patient refused to answer vs. Less than 50 GHC	5.62 (0.50, 63.28)	1.23	0.16	2.82 (0.22, 36.01)	1.30	0.43
50–300 GHC vs. Patient refused to answer	0.33 (0.03, 3.19)	1.16	0.34	0.59(0.05, 6.54)	1.23	0.67
Greater than 300 GHC vs. Patient refused to answer	0.38 (0.04, 3.80)	1.17	0.41	0.53 (0.05, 5.90)	1.23	0.60
Distance from Clinic/Hospital						
0 – 20 kilometers vs. More than 20 kilometers	0.50 (0.30, 0.80)	0.24	0.004	0.49 (0.30, 0.80)	0.25	0.004 *

Footnote:

* p<0.05 is considered statistically significant