

Adherence to antiretroviral therapy among children under five years in Jinja, Uganda, assessed using a combined measure

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Abstract

Background: Adherence to Anti-Retroviral Therapy (ART) is required to achieve HIV viral load suppression but children under five years in Jinja, Uganda, had been shown to have low HIV suppression rates. This study aimed to determine the level of ART non-adherence among these children and the associated factors.

Methods: Data for the cross-sectional study was obtained from caregivers of 206 HIV positive children under five years attending health facilities in Jinja who had been on ART for at least three months. Non-adherence was measured using a Visual Analog Scale that assessed both dosing and timing non-adherence, and by determining the Proportion of Days Covered by the medication. A questionnaire administered to the caregivers was used to collect the data, together with medical record review. A child was only considered adherent if they had adherence greater than 95% on both measures. The data was analysed using Modified Poisson Regression, taking a p-value less than 0.05 as statistically significant.

Results: Of the 206 children, 73.8% were older than 2 years, and 52.9% were female. Likewise, the majority of the caregivers were female (93.7%). According to the combined adherence measure, 51.5% of the children were categorized as non-adherent. School attendance, Prevalence Ratio (PR) = 1.32 ($p = 0.024$), receiving financial support from family, PR = 0.68 ($p = 0.026$) and satisfaction with the quality of service at the health facility, PR = 0.96 ($p < 0.001$) were associated with non-adherence. Household food insecurity was also associated with non-adherence: PR = 1.63 ($p = 0.007$) for mild food insecurity, PR = 1.67 ($p = 0.006$) for moderate insecurity and PR = 1.59 ($p = 0.006$) for severe food insecurity.

Conclusions: Children under five years in Jinja had a high level of ART non-adherence. It is important to engage schools to support adherence among children living with HIV. Addressing household food insecurity would also reduce the barriers to optimal adherence.

Background

Since its introduction, Anti-Retroviral Therapy (ART) has gradually led to a reduction in the number of HIV related deaths globally (1), and the World Health Organization (WHO) recommends treatment for all people diagnosed with HIV regardless of clinical stage (2). In Uganda all children with confirmed HIV are started on ART at the earliest opportunity, regardless of clinical stage, to suppress the viral load to undetectable levels (3). Perfect or near perfect adherence to ART, defined as adherence over 95%, is required to achieve full viral load suppression (4). However, viral load suppression is lowest among children under 15 years in Uganda at 39.3% compared with 59.6% among those 15 years and older (5). In Jinja district, specifically, HIV suppression rates recorded among children under five years between January and October, 2018 were below the national target of 90% at 58.0%, and lower than the 71.8% recorded for children 5 to 14 years old and the 89.7% for patients 15 years and older(6).

A study done in Western Uganda assessing paediatric ART adherence found that children older than 10 years were more likely to adhere to ART than the younger ones (7). Factors like caregiver's knowledge

of their HIV status and differences between health facilities were found to influence adherence (7). Haberer, Kiwanuka (8) also found hospitalization of the child, liquid formulation use and caregiver alcohol use to be associated with less than 90% adherence among children aged 2 to 10 years in Western Uganda. However, most research on paediatric ART adherence done in Uganda and elsewhere has mostly been among adolescents (9, 10), and for studies that include children under five, these children have been grouped together with the older ones (7, 8). This has the potential of disguising adherence challenges specific to children under five. Moreover, self-reports were the prevalent measure of non-adherence used, and yet, given the limitations of the different adherence measures, WHO recommends a multi-method approach to measuring ART non-adherence(11).

This study therefore aimed to determine the level of ART non-adherence among children under the age of five in Jinja district using an objective and a subjective measure of adherence so as to increase the likelihood of identifying non-adherence. The study also intended to determine the child, caregiver, drug regimen and health system factors that influence this non-adherence. The findings from the study are expected to contribute to understanding barriers to optimal ART adherence among these children and guide the design of interventions to address them.

Methods

Study setting

Data was collected from April to July, 2019, in health facilities in Jinja that offer paediatric ART services. Jinja is a district in the south-eastern part of Uganda with a population of about 471,242 people (12). At the district level, the public health system in Uganda is decentralized with Village Health Teams making up the lowest level, followed by Health Centre II facilities (HCII's), HCIII's, HCIV's and the district and regional hospitals. Data was collected from Jinja Regional Referral Hospital, 2 Non-Government Organization-run health facilities, the 5 HCIV's and 9 HCIII's. These health facilities all provide paediatric ART services at no charge.

Study design

A cross-sectional study design was used. Quantitative data was collected through a health facility-based survey and medical record review.

Participants

The study population was HIV positive children under five years who had been on ART for at least three months and were receiving ART services from health facilities in Jinja. The respondents were the caregivers with whom the children presented to the health facilities on the days of data collection. Only children who had lived with their caregiver for at least one month were included in the study. These were sampled consecutively as they were presented for care and, for caregivers with more than one eligible child, the first child to be presented was included. Eligible children whose caregivers declined to give consent to participate were excluded from the study.

Data collection, variables and their measurement

An interviewer-administered electronic questionnaire was used to collect data from eligible caregivers using KoBo Toolbox kit (13) installed on mobile phones. The questionnaire was provided in English and also translated into Lusoga, the language predominantly spoken in Jinja. Data was extracted from medical records of children whose caregivers had been interviewed using an electronic data abstraction form. The study tools had been pretested on five children in a health facility in a neighbouring district.

The outcome variable, non-adherence to ART, was measured using a Visual Analogue Scale (VAS) and the Proportion of Days Covered (PDC). The VAS was based on the modified Medication Adherence Self-Report Inventory questionnaire which includes two VAS items: one part measures how much of the prescribed medicine is taken while the second part measures how much of it is taken within 2 hours of the recommended time over 30 days. (14) An average VAS score was then obtained for the two scales. Through medical record review, concurrent adherence to all medicines in the ART regimen for each child was also determined by calculating the PDC, the proportion of days over a 90-day period when the child had supply of all drugs in their ART regimen. Adherence was categorized at the 95% cut-off on both the average VAS score and the PDC measure, and only children with adherence levels of 95% or greater on both measures were considered adherent.

Data was also collected on the exposure variables: the child, drug regimen, health system and caregiver factors. The child factors were age, gender, place of delivery, school/day-care attendance, illness in the past two weeks and clinical stage on ART initiation, which were measured using the questionnaire. The child's most recent viral load reading before the date of data collection was recorded from their medical records. Data on drug regimen factors including the drug combination the child was on, the experience of side effects and drug regimen changes since ART initiation was obtained from medical records. Health system factors were measured using the questionnaire. These included: the type of health facility, the physician-patient relationship which was measured using 13 items from the Patient Communication Behaviours Scale (15) and the caregiver satisfaction with the quality of service at the child's ART clinic, assessed using a 9-item scale adopted from Ivy, Ng (16).

The caregiver factors were assessed through the questionnaire and they included: age, sex, highest education level attained, marital status, place of residence, HIV status, relation to the child, main source of financial support, beliefs about medicine, alcohol use and household food security. The caregiver's beliefs about medicine were assessed using 10 questions from the 18-item Beliefs About Medicine questionnaire (BMQ) (17). These included 5 questions assessing beliefs about necessity of the medicine (BMQ-Necessity scale), and 5 questions assessing concerns about the medicine's negative effects (BMQ-Concern scale). Statements in the BMQ were scored on a Likert-type scale that ranged from 1, for strongly disagree to 5, for strongly agree. The maximum score on both the BMQ-Necessity and BMQ-Concern scales was 25, and using a cut-off of 12.5, caregiver beliefs about medicine could be classified as "Accepting", "Ambivalent", "Indifferent" or "Skeptical". (18, 19). Household food security was measured

using the Household Food Insecurity Access Scale (HFIAS), which categorized households as “Food secure”, “Mildly food insecure”, “Moderately food insecure” or “Severely food insecure” (20).

Study size

The formula for sample size determination of cross-sectional studies (21) was used to estimate the number of children to sample, using an estimated prevalence of ART non-adherence of 21% (7), a precision of 5%, and adjusted for a finite population of 305, the number of children active on ART in Jinja as of September, 2018. The final sample size was then adjusted for non-response of 20% to give a minimum sample size of 168 children.

Statistical analysis

Data was analysed using STATA version 14 (StataCorp LP, TX, USA). Means with standard deviations were used to summarize normally distributed continuous variables while medians with interquartile ranges were used for continuous variables that were non-normally distributed. Frequencies and their corresponding percentages were used for the categorical variables. The outcome variable, non-adherence measured by the combined average VAS and PDC measures, was presented as a proportion.

Modified Poisson Regression was used for bivariate and multivariable analysis and associations were measured using Prevalence Ratios (PRs). Exposure variables with p-values less than 0.1 at bivariate analysis were considered for inclusion into the multivariable analysis model. Multi-collinearity between the candidate variables was examined and a correlation coefficient greater than 0.4 was considered high collinearity. Stepwise elimination was used to build the multivariable model, where elimination and addition of variables was based on the Akaike Information Criteria and variables specified as important from previous literature. Agreement between the two measures of non-adherence used, the VAS and PDC, was determined using the kappa statistic. A p-value less than 0.05 was considered statistically significant for all analyses.

Results

Characteristics of the study participants

A total of 206 children under five years were included in the study. The majority of the children (73.8%) were older than 2 years, 109 (52.9%) of them were female and 72 (34.9%) were in school/day-care (Table 1). Of the 129 (62.6%) who had a viral load record, 55.8% had their most recent viral load recorded as less than 1000 copies/ml. Out of the 206 caregivers interviewed, 48.1% were aged between 25 to 34 years, and 193 (93.7%) of them were female. Only 50 (24.3%) of the caregivers were unemployed. The majority (73.8%) were the biological parents of the children they had presented for care. Most were HIV positive (79.1%), and of these 98.8% were on ART.

Table 1

Child and caregiver descriptive characteristics (n = 206)

Characteristic	Frequency (%)
Children	
Age (months)	
6 to 24	54 (26.2)
25 to 59	152 (73.8)
Health facility type	
Public health facility	142 (68.9)
NGO health facility	64 (31.1)
Current ART regimen	
ABC + 3TC + LPV/r	124 (60.2)
Other ABC-based regimen ^a	50 (24.3)
Other AZT-based regimen ^b	32 (15.5)
Duration on ART (months)	
Median (IQR)	18.5 (20.7)
Most recent viral load (N = 129)	
< 1000 copies/ml	72 (55.8)
≥ 1000 copies/ml	57 (44.2)
Caregivers	
Age (years)	
18 to 24	41 (19.9)
25 to 34	99 (48.1)
35 to 44	44 (21.3)
45 to 70	22 (10.7)
Highest education level attained	
None	19 (9.2)
Primary	90 (43.7)
Secondary	87 (42.2)

Characteristic	Frequency (%)
Tertiary	10 (4.9)
Marital status	
Never married	28 (13.6)
Living with partner but not married	124 (60.2)
Married	10 (4.8)
Divorced/Separated	35 (17.0)
Widow/Widower	9 (4.4)
Residence	
Rural	128 (62.1)
Urban	78 (37.9)
Monthly income (Uganda shillings)	
< 130,000	93 (67.4)
≥ 130,000	45 (32.6)
HIV Status	
Positive	163 (79.1)
Negative	40 (19.4)
Didn't Know	3 (1.5)
HIV positive and on ART (n = 163)	
Yes	161 (98.8)
No	2 (1.2)
Relation to the child	
Biological parent	152 (73.8)
Other blood relative	17 (8.2)
Non-blood relation	37 (18.0)
Alcohol use in the last 30 days	
Never	192 (93.2)
Ever used	14 (6.8)

Characteristic	Frequency (%)
^a ABC + 3TC + EFV, ABC + 3TC + NVP	
^b AZT + 3TC + LPV/r, AZT + 3TC + NVP, AZT + 3TC + EFV	

Level of non-adherence to ART

Using the 30-day VAS scale, 38.4% of the caregivers reported having given the children less than 95% of their doses (VAS-dose) while 53.4% of them had not administered their children’s medicine within 2 hours of the correct time (VAS-timing). According to the average VAS score, 47.1% of the children were classified as having an adherence level less than 95%. Using the PDC measure, 16.5% of the children were covered less than 95% of the days by their ART medication in the past 90 days. Applying the combined average VAS score and the PDC measures, 51.5% of the children were found to be non-adherent. The average VAS score and the PDC only had slight agreement with a kappa statistic of 0.18 ($p < 0.001$), although their percentage agreement was at 60.7%.

Healthcare providers in Uganda also routinely assess and record adherence at every child’s clinic visit, and from record review, only 5.8% of all the children included in this study had been categorized by their healthcare providers at their most recent visit as having an adherence level below 95%.

Factors associated with non-adherence

At bivariate analysis, only school/day-care attendance was significantly associated with non-adherence among the child factors (Table 2). Caregiver factors significantly associated with non-adherence at bivariate analysis were caregiver positive HIV status, receiving financial support from the partner as opposed to relying on the caregiver’s income and household food insecurity. Among the health system factors, type of health facility and caregiver satisfaction with the quality of care at the health were significantly associated with non-adherence at bivariate analysis. None of the drug regimen factors were significantly associated with non-adherence at this level.

Table 2
Factors associated with non-adherence at bivariate analysis.

	Adherent (n = 100)	Non- adherent (n = 106)			
Factor	n (%)	n (%)	Unadjusted PR	Confidence Interval	p- value
Child factors					
Age (months)					
6 to 24	29 (53.7)	25 (46.3)	1		
25 to 59	71 (46.7)	81 (53.3)	1.15	(0.83–1.59)	0.395
Gender					
Female	58 (53.2)	51 (46.8)	0.83	(0.63–1.08)	0.157
Male	42 (43.3)	55 (56.7)	1		
Place of delivery					
Home	10 (38.5)	16 (61.5)	1		
Public Health Facility	62 (55.9)	49 (44.1)	0.72	(0.50–1.04)	0.078
Private Health Facility	21 (44.7)	26 (55.3)	0.9	(0.60–1.34)	0.601
Didn't know	7 (31.8)	15 (68.2)	1.11	(0.73–1.68)	0.631
School/Day care attendance					
No	75 (56.0)	59 (44.0)	1		
Yes	25 (34.7)	47 (65.3)	1.48	(1.15–1.91)	0.002
Illness in the past two weeks					
No	71 (49.6)	72 (50.4)	1		
Yes	29 (46.0)	34 (54.0)	1.07	(0.81–1.42)	0.628

	Adherent (n = 100)	Non- adherent (n = 106)			
Clinical stage on ART initiation					
I	47 (50.0)	47 (50.0)	1		
II	21 (55.3)	17 (44.7)	0.9	(0.60–1.35)	0.593
III	8 (32.0)	17 (68.0)	1.36	(0.97–1.91)	0.074
IV	2 (25.0)	6 (75.0)	1.5	(0.96–2.35)	0.077
Caregiver factors					
Age (years)					
18 to 24	25 (61.0)	16 (39.0)	1		
25 to 34	43 (43.4)	56 (56.6)	1.45	(0.95–2.21)	0.084
35 to 44	19 (43.2)	25 (56.8)	1.46	(0.92–2.31)	0.111
45 to 70	13 (59.1)	9 (40.9)	1.05	(0.56–1.97)	0.884
Sex					
Female	96 (49.7)	97 (50.3)	0.73	(0.49–1.07)	0.107
Male	4 (30.8)	9 (69.2)	1		
Highest education level attained					
None	10 (52.6)	9 (47.4)	1		
Primary	42 (46.7)	48 (53.3)	1.13	(0.67–1.88)	0.651
Secondary	40 (46.0)	47 (54.0)	1.14	(0.68–1.91)	0.616
Tertiary	8 (80.0)	2 (20.0)	0.42	(0.11–1.60)	0.204
Marital status					
Never married	15 (53.6)	13 (46.4)	1		

	Adherent (n = 100)	Non- adherent (n = 106)			
Living with partner but unmarried	63 (50.8)	61 (49.2)	1.06	(0.68–1.64)	0.795
Married	3 (30.0)	7 (70.0)	1.51	(0.85–2.67)	0.158
Divorced/Separated	15 (42.9)	20 (57.1)	1.23	(0.75–2.01)	0.408
Widow/Widower	4 (44.4)	5 (55.6)	1.2	(0.59–2.43)	0.620
Residence					
Rural	60 (46.9)	68 (53.1)	1		
Urban	40 (51.3)	38 (48.7)	0.92	(0.69–1.21)	0.545
HIV Status					
Negative	14 (35.0)	26 (65.0)	1		
Positive	84 (51.5)	79 (48.5)	0.75	(0.57–0.98)	0.038
Didn't Know	2 (66.7)	1 (33.3)	0.51	(0.10–2.59)	0.419
Relation to the child					
Biological parent	77 (50.7)	75 (49.3)	1		
Other blood relative	10 (58.8)	7 (41.2)	0.84	(0.46–1.51)	0.549
Non-blood relation	13 (35.1)	24 (64.9)	1.31	(0.99–1.75)	0.062
Main source of financial support					
From income	22 (36.7)	38 (63.3)	1		
From family	25 (55.6)	20 (44.4)	0.7	(0.48–1.03)	0.068
From partner	49 (52.7)	44 (47.3)	0.75	(0.56–1.00)	0.048
From friends and charities	4 (50.0)	4 (50.0)	0.79	(0.38–1.62)	0.520

	Adherent (n = 100)	Non- adherent (n = 106)			
Beliefs about medicine					
Ambivalent	76 (52.4)	69 (47.6)	1		
Accepting or indifferent	24 (39.3)	37 (60.7)	1.28	(0.98 – 0.40)	0.073
Alcohol use in the last 30 days					
Never	96 (50.0)	96 (50.0)	1		
Ever used	4 (28.6)	10 (71.4)	1.43	(1.00–2.05)	0.053
Household food security					
Food secure	65 (63.7)	37 (36.3)	1		
Mild insecurity	9 (30.0)	21 (70.0)	1.93	(1.36–2.74)	< 0.001
Moderate insecurity	11 (31.3)	15 (57.7)	1.59	(1.05–2.42)	0.030
Severe insecurity	15 (31.3)	33 (68.7)	1.9	(1.38–2.61)	< 0.001
Drug regimen characteristics					
ART regimen currently on					
ABC + 3TC + LPV/r	56 (45.2)	68 (54.8)	1		
Other ABC-based regimen	29 (58.0)	21 (42.0)	0.77	(0.53–1.10)	0.151
Other AZT-based regimen	15 (46.9)	17 (53.1)	0.97	(0.67–1.39)	0.864
ART regimen change					
No	52 (51.0)	50 (49.0)	1		
Yes	48 (46.2)	56 (53.8)	1.1	(0.84–1.43)	0.49
Side effects reported					

	Adherent (n = 100)	Non- adherent (n = 106)			
No	91 (47.6)	100 (52.4)	1		
Yes	9 (60.0)	6 (40.0)	0.76	(0.41–1.44)	0.407
Health system factors					
Health facility					
Public health facility	50 (35.2)	92 (64.8)	1		
NGO health facility	50 (78.1)	14 (21.9)	0.34	(0.21–0.55)	< 0.001
Physician-patient relationship					
Mean score (S.D)	61.6 (8.9)	61.4 (4.7)	1	(0.98–1.02)	0.851
Satisfaction					
Mean score (S.D)	83.5 (6.9)	78.4 (7.0)	0.96	(0.95–0.98)	0.001

Six variables were included in the final multivariable analysis model: age of the caregiver, household food security, caregiver satisfaction with the quality of service at the health facility, main source of financial support, school/day-care attendance by the child and the child's place of delivery (Table 3). After controlling for other variables, among the child factors, only school/day-care attendance was significantly associated with non-adherence: children who were in school/day-care were 1.32 times as likely to be non-adherent as compared to those who were not in school/day-care ($p = 0.024$; 95% C.I.: 1.04, 1.69).

Caregivers whose main source of financial support was from family were 0.68 times as likely to have a non-adherent child as compared to those whose main source of financial support was from their income ($p = 0.026$, 95% C.I.: 0.49, 0.96). Non-adherence was also found to be more prevalent in households with food insecurity. The prevalence increased with increasing food insecurity from a PR of 1.63 ($p = 0.007$, 95% C.I.: 1.15, 2.32) for those with mild food insecurity; to a PR of 1.67 ($p = 0.006$, 95% C.I.: 1.16, 2.42) for moderate food insecurity. However, households with severe food insecurity had a lower prevalence of non-adherence, PR = 1.59 ($p = 0.006$, 95% C.I.: 1.14, 2.22), as compared to those with mild and moderate food insecurity.

Satisfaction with the quality of services at the child's ART clinic was the only health system factor significantly associated with non-adherence. The more satisfied a caregiver was with the quality of

services at the health facility their child attended, the less likely their child was to be non-adherent to their ART medication, PR = 0.96 (p-value < 0.001; 95% C.I.: 0.95, 0.98).

Table 3
Factors associated with non-adherence at multivariable analysis

Factor	Unadjusted PR	Confidence interval	p-value	Adjusted PR	Confidence interval	p-value
Caregiver age (years)						
18 to 24	1			1		
25 to 34	1.45	(0.95–2.21)	0.084	1.39	(0.94–2.05)	0.096
35 to 44	1.46	(0.92–2.31)	0.111	1.18	(0.77–1.81)	0.460
45 to 70	1.05	(0.56–1.97)	0.884	0.78	(0.41–1.49)	0.456
Place of delivery						
Home	1			1		
Public Health Facility	0.72	(0.50–1.04)	0.078	0.67	(0.45–1.01)	0.057
Private Health Facility	0.90	(0.60–1.34)	0.601	0.85	(0.55–1.30)	0.448
Didn't know	1.11	(0.73–1.68)	0.631	1.21	(0.78–1.90)	0.385
School/Day-care attendance						
No	1			1		
Yes	1.48	(1.15–1.91)	0.002	1.32	(1.04–1.69)	0.024
Main source of financial support						
From income	1			1		
From family	0.70	(0.48–1.03)	0.068	0.68	(0.49–0.96)	0.026
From partner	0.75	(0.56–1.00)	0.048	0.8	(0.60–1.08)	0.145
From friends and charities	0.79	(0.38–1.62)	0.52	0.54	(0.26–1.11)	0.092
Household food security						
Food secure	1			1		
Mild insecurity	1.93	(1.36–2.74)	< 0.001	1.63	(1.15–2.32)	0.007
Moderate insecurity	1.59	(1.05–2.42)	0.03	1.67	(1.16–2.42)	0.006
Severe insecurity	1.90	(1.38–2.61)	< 0.001	1.59	(1.14–2.22)	0.006

Factor	Unadjusted PR	Confidence interval	p-value	Adjusted PR	Confidence interval	p-value
Satisfaction with the quality of care						
Mean score	0.96	(0.95–0.98)	< 0.001	0.96	(0.95–0.98)	<0.001

Discussion

This study aimed to determine the level of non-adherence to ART among children under five years in Jinja district, Uganda, and the factors associated with it. Inasmuch as optimal adherence is important for achieving viral load suppression and delaying emergence of drug resistance, findings from the study showed children under five years in Jinja to have a high level of non-adherence to ART. Non-adherence was more prevalent among children who attended school/day-care and those from households with food insecurity, and less among children with caregivers receiving financial support from family members and those with increased satisfaction with the quality of service received at the child's ART clinic.

Most previous paediatric ART adherence research has studied children under five years combined with children of older age groups, using cut-offs varying from 80–95%. Most of these studies have also reported lower levels of non-adherence than what was found in this study. Wadunde, Tuhebwe (7) studied children aged 0 to 14 years in Western Uganda and found the level of non-adherence to be 21% using self-reports at a 90% cut off. This is similar to the 30% found among 2 to 19 year old children in Tanzania at an 80% cut-off using pill counts (22), and the 9.7% among children under 15 years in Ethiopia using self-reports at a 95% cut-off (23). Davies, Boulle (24) also reported a lower non-adherence level among children under five years in South Africa using medicine return at a 90% cut-off. However, studies that utilized combined measures of adherence were able to identify more non-adherent children and found similarly high levels of non-adherence as was found in our study. Nsheha, Dow (25) found non-adherence among children aged 2 to 17 years in Tanzania to be as high as 75.4% when they were subject to three measures of adherence: a two-day self-report, a one-month VAS and unannounced pill counts.

Differences were observed between the two adherence measures used. More children were categorized as non-adherent by VAS than PDC, suggesting that many caregivers collect the ART medicines for their children from the clinics but fail to administer them at home. Providing ART at no cost in ART clinics in Uganda eliminates the biggest financial barrier to access, even if other barriers at home still prevail. It is also notable that healthcare providers during routine practice were only able to identify a few of the non-adherent children implying that relying on appointment keeping at the clinics alone to measure non-adherence, as is the practice in Uganda, may not be sufficient to identify and support non-adherent children.

Children who were in school/day-care were found to be more likely to be non-adherent and this could be attributed to the differences in daily schedules between these children and their caregivers, which make it easy for doses to be skipped. Moreover, even if the caregiver remembers to administer the drugs after the

scheduled dosing time, there would be no way of quickly administering the drug if the child has already left for school/day-care. The stigma faced by HIV positive children and their caregivers also makes it hard for the caregivers to entrust school teachers to help with administering the medicine at school. Nyogea, Mtenga (22) found unfavourable school environments to be a barrier to optimal adherence among children on ART in Tanzania.

Food insecurity was found to be associated with non-adherence and this would be expected as caregivers who are afraid of effects of administering food on an empty stomach skip their children's doses as they wait for food to be available. This finding is also similar to what Ndayikeje, Wilson (26) found in Rwanda where lack of food to take with tablets was associated with non-adherence to ART among children aged 1 to 18 years. However, contrary to the expectation, we found households with severe food insecurity to be less likely to have non-adherent children than those with mild and moderate food insecurity. According to the HFIAS, households with severe food insecurity experience frequent cut-backs on meal sizes and frequencies and often run out of food (20). It is possible that such households have fallen into a more predictable food shortage routine and adapted better than those with mild and moderate food insecurity. As such, the effects of food insecurity on their children's adherence is less pronounced than that of household with mild and moderate insecurity. Nonetheless, their children were still more likely to be non-adherent than those from households with secure food access.

As would be expected, children of caregivers who were satisfied with the quality of service at the health facilities were less likely to be non-adherent. The scale used to measure satisfaction with the quality of service at the health facility measured attributes such as the physical environment, pharmacy service, waiting time and the way the healthcare provider related with the children and caregivers. Good quality services motivate caregivers to keep appointments to collect medicine. Nabukeera-Barungi, Elyanu (9) also found supportive health care workers and short waiting time at the health facility to be facilitators of adherence among adolescents in Uganda. It is however surprising that none of the drug regimen characteristics were significantly associated with non-adherence as these had been reported in previous studies (22, 24, 26).

Caregivers whose main source of financial support was from their family were less likely to have non-adherent children than those who relied on their jobs. It is possible that those who rely on their jobs are at times forced to work longer hours to be able to provide for their families adequately, and if they do not have enough social support, may fail to administer medicine to their children in time

Study Limitations

A VAS is a subjective measure and is prone to reporting bias which may have underestimated non-adherence, especially as the data was obtained from caregivers. Drug refill data also assumes that all collected medicine is administered as instructed, and this may have also underestimated non-adherence. On the other hand, drug refill data may fail to reveal previous excess refills which may assume non-

adherence where there is none, and thus overestimate non-adherence. Nonetheless, using the two measures combined together in this study increased the ability of the study to identify non-adherence.

Conclusions

Findings from this study revealed that children under five years in Jinja district had a high level non-adherence to ART. School attendance and food insecurity were found to be associated with increased non-adherence while increased satisfaction with the quality of services at health facilities and depending on financial support from family were associated with reduced non-adherence to ART among these children.

It is therefore important to engage schools and day-care centres to support adherence to ART among young children living with HIV and to ensure continuous adherence to therapy even when the child is at school/day-care. The caregivers should also be empowered economically to guarantee food security. These should also be educated on less costly child feeding practices to ensure that children are tended to even in times of food scarcity. At the health facilities, constant review and improvement of paediatric ART clinic services should be prioritized to further minimise the barriers to adherence within the health system.

Abbreviations

3TC: Lamivudine; ABC: Abacavir; AIDS: Acquired Immune Deficiency Syndrome; ART: Antiretroviral therapy; EFV: Efavirenz; HFIAS: Household Food Insecurity Access Scale; HIV: Human Immunodeficiency Virus; LPV/r: Ritonavir-boosted Lopinavir; NVP: Nevirapine; PDC: Proportion of Days Covered; VAS: Visual Analog Scale; WHO: World Health Organization.

Declarations

Ethics approval and consent to participate

Ethics approval for the study was sought from Makerere University School of Public Health Higher Degrees Research and Ethics Committee. Administrative clearance was also obtained from the Jinja District Health Office and the individual health facilities from which data was collected.

For all children included in the study, written informed consent was obtained from their parents or guardians who they presented with to the health facility. The parents and guardians could provide consent if they were 18 years and older, or if they were considered emancipated minors.

Consent for publication

Written informed consent for publication of study findings using de-identified data was sought from all caregivers of children involved in the study.

Availability of data and materials

Data analysed during this study can be made available to all interested researchers upon reasonable request directed to the corresponding author, Ms. Jacquelyn Nambi Ssanyu (sanyukajacque@gmail.com).

Competing interests

The authors declare that they have no competing interest.

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Authors' contributions

JNS conceived the study, wrote the study protocol, participated in data collection, analysed the data and wrote the first draft of the manuscript. MN and FN supported and guided JNS in conceptualizing and designing the study, analysing data, interpreting results and reviewing the draft manuscript. All authors read and approved the final manuscript.

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