Factors Associated with Nonadherence to Antiretroviral Therapy among Children with HIV/AIDS in Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

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Abstract

Background: The advent of antiretroviral (ARV) treatment in combined therapy has transformed HIV/AIDS into a chronic treatable condition and significantly improved the prognosis and quality of life of patients with HIV/AIDS. However, to achieve this, patients have to maintain strict adherence which has been shown to be affected by several factors. This study, therefore, aimed to estimate and identify factors associated with adherence to ARV drugs among children attending Paediatric ARV Clinic at Ahmadu Bello University Teaching Hospital, Zaria. **Subjects and Methods:** Sociodemographic and clinical information of the children and their caregivers was collected using a semi-structured questionnaire. Bivariate and multivariate analyses were done to examine the odds of adherence and nonadherence to ARV therapy with respect to the various factors. $P = 0.05$ was considered statistically significant. **Results:** A total of 167 children and their caregivers were studied. The children were aged between 2 and 17 years with a mean age of 9.1 ± 3.4 years, while the caregivers were aged between 20 and 70 years with a mean age of 37.6 ± 10.7 years. The estimated adherence in the past 30 days was found to be 76.6%. Caregivers' forgetfulness and traveling were reported as the major reasons for missing medications. Caregivers' age <35 years was significantly associated with poor adherence (odds ratio = 2.35 [95% confidence interval: 1.09–5.06]). **Conclusion:** Caregiver factors were the main factors associated with poor adherence in children with HIV. We recommend regular adherence counseling at every visit with emphasis on the use of reminder methods to improve adherence.

Keywords: Adherence, antiretroviral therapy, caregivers, children, self-reporting

Introduction

HIV/AIDS is one of the world's most significant public health challenges of this century, especially in developing countries.[1] Majority of HIV infections occur in sub-Saharan Africa. Nigeria has the second-largest number of people living with HIV/AIDS (PLWHA) in the world with a total of 3.4 million PLWHA with about 1.8 million children <18 years infected which represents 90% of all children living with HIV worldwide.[1,2]

The advent of highly active antiretroviral therapy (HAART) has significantly improved the prognosis and quality of life of patients with HIV/AIDS, reducing the rate of disease progression and death.[3] This has now transformed the disease into a chronic treatable condition for a significant proportion of PLWHA who have access to ART, especially children who are now surviving into adolescence and adulthood. The antiretroviral (ARV) drugs have to be taken as a lifelong therapy and their success depends mainly on continual adherence to the medication regimen. Adherence levels of about 95% are required for successful treatment to avoid drug resistance and treatment failure.[4] The need to maintain this high level of adherence to lifelong therapy in children from an early age is one of the major challenges identified in pediatric ART programs. Several factors have been shown by different researchers to affect adherence to ART. These are grouped into

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child, caregiver, regimen, and disease characteristics.[5] These factors also differ in different places.

With scale-up pediatric ART programs in Nigeria, it has become necessary to monitor ART adherence and identify factors that can influence its success. Different methods such as assay of the drugs in blood, self-reporting, electronic drug monitoring, pill counts, and pharmacy refill records have been used to determine the level of adherence.[6] Adherence measurement in children is more complicated than measurement in adults because they do not account for the role of the caregivers and the complexity of pediatric regimens.

This study, therefore, aimed to estimate the level of adherence to ART among children with HIV/AIDS using self-report and also explore the factors associated with nonadherence to ART among children living with HIV/AIDS in Zaria, Nigeria.

Subjects and Methods

Study design and area

This cross-sectional and descriptive study was conducted at the Paediatric ARV (PARV) Clinic of Ahmadu Bello University Teaching Hospital (ABUTH) Zaria, Kaduna State. The clinic attends to an average of 30–40 patients weekly. It offers free care and treatment to all HIV-exposed and HIV-infected children presenting to the clinic. HIV and ART adherence counseling was done for the clients at presentation and before commencing ARVs.

Study population

The study involved 167 HIV-positive children between the ages of 3 months and 17 years attending the PARV Clinic of ABUTH, Zaria, who have been on ARVs for at least 3 months. Systematic random sampling technique was done to recruit participants into the study. From the list of patients attending the Paediatric HIV Clinic on Tuesdays and Thursdays obtained from the record office, every third patient is selected and included in the study. This is gotten by dividing the total number of patients attending the clinic by the minimum sample size where the K is gotten as 3. The first patient on each clinic day was randomly selected using random number table. Thereafter, every third patient was selected until the end of the clinic. This was continued on every clinic day until the minimum sample size was reached over a period of 4 months.

Tools and method of data collection

A semi-structured interviewer-administered questionnaire was used for the study. The questionnaire has three sections. The first section contains questions on child's demographic and clinical information which includes age, sex age at diagnosis, duration on ART, type of ART, clinical stage of the disease, and WHO staging. The second section contains questions on caregiver's sociodemographic information which includes caregiver's age, sex, educational level, marital status, occupational status, HIV status, caregiver's relation with child, and whether the caregiver is also on ART. The last section contains information relating to medication adherence which includes number of tablets given, number of doses per day, number of doses missed, reasons for missing the dose/s, remember mechanism for time of medication, and whether the medications were switched or not and number of times switched. The data were collected by the researcher and two trained research assistants, who are community health officers, using face-to-face interview.

The adherence level was measured using caregivers' report of 1-month recall of medication use. The level of adherence was classified into those with good adherence of greater than or equal to 95% and those with poor adherence of <95%. A child is said to have adherence of <95% if he missed 3 or more doses within the month.

Those who were on zidovudine, lamivudine, and nevirapine or zidovudine, lamivudine, and efavirenz were classified as being on first-line ARV drugs, while those on abacavir, lamivudine, and lopinavir-boosted ritonavir were considered on second line. Nutritional status was determined using weight for age. Those with weight for age of >80% of expected were classified as normal, while those with weight for age of <80% were classified as malnourished.

Data management and analysis

Data obtained were entered into and analyzed using Epi Info statistical software (version 3.5.4). Descriptive statistic was carried out to analyze the sociodemographic and clinical characteristics of the patients and the adherence rate. Bivariate analysis was done to find the association between exposure variables and adherence. Logistic regression was also performed for variables which showed a statistically significant association in the bivariate analysis. $P = 0.05$ was considered statistically significant.

Ethical consideration

Approval of the Health Research Ethical Committee of Ahmadu Bello University Teaching Hospital, Zaria, was obtained before the commencement of the study. Written informed consent was obtained from each child's parent or caregiver before recruitment into the study. Assent was obtained from children aged 7 years and beyond. The parent or caregiver did not bear any cost for the research. All the provisions of the Helsinki Declaration were duly observed.

Results

Sociodemographic and clinical characteristics of children and their caregivers

A total of 167 primary caregivers were interviewed. The caregivers' ages were between 20 and 70 years with a mean of 37.6 ± 10.7 years, 153 (91.6%) of whom were females and 117 (70.1%) were married. The majority of the caregivers 122 (73.1%) were biological parents of the children and 129 (77.2%) had at least primary level of education, but less than a quarter of them 39 (23.4%) were gainfully employed [Table 1]. All the caregivers reported having

Table 1: Caregivers' sociodemographic and clinical characteristics and adherence to antiretroviral therapy, Ahmadu Bello University Teaching Hospital, Zaria, 2015

Variable	All caregivers	Adherence		OR (95% CI)	*P*
		<95%	≥95%		
Caregiver's age (years)					
<35	74 (44.3)	23 (31.1)	51 (68.9)	2.21 (1.05-4.50)	0.04
≥35	93 (55.7)	16 (17.2)	77 (82.8)		
Primary caregiver					
Parents	122 (73.1)	22 (18.0)	100 (82.0)	0.36 (0.17-0.77)	0.007
Others	45 (26.9)	17 (37.8)	28 (62.2)		
Caregiver's sex					
Female	153 (91.6)	36 (23.5)	117 (76.5)	1.12 (0.30-4.27)	0.86
Male	14 (8.4)	3 (21.4)	11 (78.6)		
Marital status					
Not married	50 (29.9)	12 (24.0)	38 (76.0)	1.05 (0.48-2.29)	0.90
Married	117 (70.1)	27 (23.1)	90 (76.9)		
Educational level					
At least primary	129 (77.2)	35 (27.1)	94 (72.9)	3.16 (1.05-9.56)	0.03
No education	38 (22.8)	4 (10.5)	34 (89.5)		
Occupational status					
Employed	39 (23.4)	15 (38.5)	24 (61.5)	2.71 (1.24-5.93)	0.01
Unemployed	128 (76.6)	24 (18.8)	104 (81.2)		
Caregiver HIV status					
Negative	44 (27.0)	15 (34.1)	29 (65.9)	2.28 (1.05-4.96)	0.03
Positive	119 (73.0)	22 (18.5)	97 (81.5)		
Caregiver on HAART					
No	49 (29.3)	17 (34.7)	32 (65.3)	2.32 (1.10-4.90)	0.03
Yes	118 (70.7)	22 (18.6)	96 (81.4)		

HAART: Highly active antiretroviral therapy, OR: Odds ratio, CI: Confidence interval

received adherence counseling prior to commencement of the ARV drugs.

Table 2 shows the characteristics of the children. The ages of the children were between 2 and 17 years, with a mean of 9.1 ± 3.3 years. Seventy-four (44.3%) of the children were between 5 and 9 years, while only 7 (4.2%) were 15 years and above. More than half of the children 86 (51.5%) were females. Of the 167 children studied, 76 (46.1%) were orphans, out of which 21 (12.6%) were double orphans.

Only 19 (11.4%) children knew their HIV status and all were aged above 7 years. Forty-eight (28.7%) of the children were malnourished. Majority of the children 99 (59.3%) were in WHO stages I and II. Most of the children 155 (92.8%) were on first-line drugs, with 84 (50.3%) being on the drugs for more than 5 years, and only 6 (3.6%) were on the ART for more than 10 years. Fourteen (8.4%) of the children on ART had their drugs switched at least once.

Adherence to antiretroviral therapy

A total of 128 (76.6%) children had adherence of at least 95% as assessed by caregivers' recall over the last 1 month before interview, while 110 (65.9%) had 100% adherence during the same period [Table 3].

Figure 1 shows the reasons for missing medications. The most common reasons given for missing at least one dose of

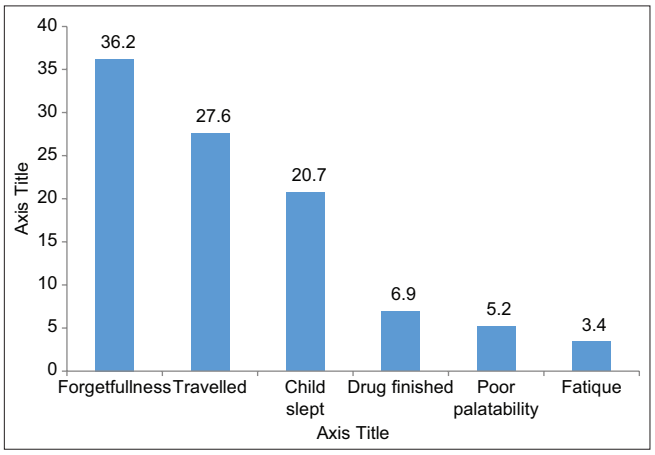

Figure 1: Caregivers' reasons for child nonadherence to antiretroviral drugs at ABUTH, Zaria, 2015

ARV drugs were forgetfulness 21 (36.2%), caregiver traveled 16 (27.6%), child slept 12 (20.7), and drug finished 4 (6.9%).

The methods used by the parents as a reminder to give their children ARV drugs are shown in Figure 2. Sixty-seven (40.1%) of the caregivers had no form of memory aid for taking ARVs, 55 (33.0%) of the caregivers used alarm as a memory aid, while forty-five (26.9%) said that other individuals reminded them to give their children's medications.

Bivariate analysis of factors associated with adherence to antiretroviral therapy in children

The caregiver-related factors associated with pediatric adherence to ART are shown in Table 1. Six of the caregiver-related factors were found to be significantly associated with poor adherence. Thirty-one percent of children whose caregivers were <35 years of age were nonadherent to HAART compared to 17.2% of children whose caregivers were 35 years of age and older (odds ratio [OR], 2.21; 95% confidence interval [CI], 1.05–4.50; P = 0.04). When we looked at relationship of caregivers to children, 37.8% of children whose caregivers were not their biological parents had significantly poor adherence when compared to 18.0% of those whose caregivers were their biological parents (OR, 0.36; 95% CI, 0.17–0.77; P = 0.007). Children whose caregivers had at least primary level of education 35 (27.1%) were less adherent to ART when compared to those whose parents had no formal education 4 (10.5%) (OR, 3.16; 95% CI, 1.05–9.56; P = 0.03).

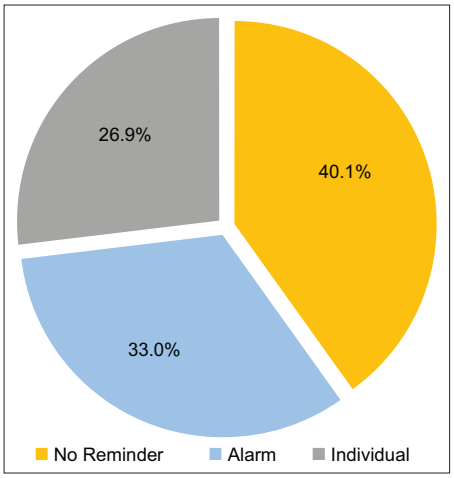

Figure 2: Caregivers' reminder methods for antiretroviral therapy adherence in children, ABUTH, Zaria, 2015

Among children whose caregivers' HIV status was negative, 34.1% were nonadherent compared to 18.5% of those whose HIV status was positive (OR, 2.28; 95% CI, 1.05–4.96; P = 0.03). Similarly, 34.7% of children whose caregivers were not on HAART were nonadherent when compared to 18.6% of those who were on HAART. This difference was also statistically significant (OR, 2.32; 95% CI, 1.05–4.96; P = 0.03). However, caregivers' sex and marital status were not significantly associated with adherence in children (OR, 1.12; 95% CI, 0.30–4.27; P = 0.86) and (OR, 1.05; 95% CI, 0.48–2.29; P = 0.09), respectively. Similarly, none of the child-related factors was found to be significantly associated with adherence to ART [Table 2].

Multivariate analysis of factors associated with adherence to antiretroviral therapy in children

After controlling for other variables, only caregivers' age <35 years was independently associated with poor adherence to ART in children (OR, 2.35; 95% CI, 1.09–5.06; P = 0.03) [Table 4].

Table 2: Child's sociodemographic and clinical characteristics and adherence to antiretroviral therapy, Ahmadu Bello University Teaching Hospital, Zaria, 2015

Variable	All children (n=167)	Adherence		OR (95% CI)	P
		<95% (n=39)	≥95% (n=128)		
Child's age					
<5	17 (10.2)	5 (29.4)	12 (70.6)	1.42 (0.47-4.32)	0.53
≥5	150 (89.8)	34 (22.7)	116 (77.3)		
Sex					
Female	86 (51.5)	19 (22.1)	67 (77.9)	0.86 (0.42-1.77)	0.69
Male	81 (48.5)	20 (24.7)	61 (75.3)		
Orphan status					
Yes	77 (46.1)	20 (26.0)	57 (74.0)	1.31 (0.64-2.69)	0.46
No	90 (53.9)	19 (21.1)	71 (78.9)		
HIV disclosure status					
Yes	148 (88.6)	36 (24.3)	112 (75.7)	1.71 (0.47-6.22)	0.41
No	19 (11.4)	3 (15.8)	16 (84.2)		
WHO stage					
I–II	99 (59.3)	23 (23.2)	76 (76.8)	0.98 (0.47-2.04)	0.96
III–IV	68 (40.7)	16 (23.5)	52 (76.5)		
Type of ART (line)					
1st	155 (92.8)	35 (22.6)	120 (77.4)	0.58 (0.17-2.05)	0.20
2nd	12 (7.2)	4 (33.3)	8 (66.7)		
Duration of ART (years)					
<5	83 (49.7)	17 (20.5)	66 (79.5)	0.73 (0.35-1.50)	0.38
≥5	84 (50.3)	22 (26.2)	62 (78.8)		

ART: Antiretroviral therapy, OR: Odds ratio, CI: Confidence interval

Table 3: Adherence assessment by caregivers' recall, Ahmadu Bello University Teaching Hospital, Zaria, 2015

Level of adherence (%)	Frequency (%)
<80	2 (1.2)
80-89	4 (2.4)
90-94	20 (12.0)
95-99	31 (18.6)
100	110 (65.9)

Table 4: Predictors of nonadherence to antiretroviral therapy among children with HIV/AIDS at Ahmadu Bello University Teaching Hospital, Zaria, 2015

Variable	AOR	95% CI	*P*
Caregiver's age (<35/≥35)	2.35	1.09-5.06	0.03
Caregiver education (none/at least primary)	0.92	0.43-2.00	0.83
Caregiver HIV status (negative/positive)	0.44	0.05-3.81	0.46
Caregiver on ART (no/yes)	0.91	0.07-12.23	0.94
Primary caregiver (others/parents)	5.69	0.52-62.81	0.16

ART: Antiretroviral therapy, AOR: Adjusted odds ratio, CI: Confidence interval

Discussion

This study examined the level of adherence to ART and the factors associated with nonadherence. The study found an estimated level of good adherence to ARV treatment of 76.6% using caregivers' report. This is similar to what was found by previous researchers from Nigeria where level of adherence to HAART among children and adolescents with HIV was reported to be between 76.1% and 86%.[7-9] In a meta-analysis where 27 studies from sub-Saharan Africa were reviewed, the average adherence when pooled was 77% which is similar to our finding.[10] Studies from Uganda and Ethiopia showed a higher prevalence of 98.1% and 93.3%, respectively.[11,12] These studies were, however, based on 3-day recall which was easier compared to our own which was based on 30-day recall. Another study from India[13] reported a higher prevalence of adherence of 86.7% in children using caregiver's recall of 30-day period similar to our study, but most of their children were on the ART for <2 years in contrast to our study where most of our patients were on the ART for more than 5 years. The implication of this finding is that about a quarter of our patients on HAART are at risk of developing drug resistance and/or treatment failure. This means that more effort has to be made to increase adherence in this group of patients.

The identified reasons for nonadherence in our study were mainly caregiver related and included forgetfulness and traveling. This finding is consistent with that of a study from Southern Nigeria which reported that nonadherence in children was primarily caregiver related.[7]

This may be because majority of our caregivers were females who have multiple responsibilities at home and so they could easily forget to ensure that their children take their medications. This finding is also similar to that of a study from Ethiopia where caregiver's forgetfulness was the major contributor to nonadherence in children.[12] Another study from India reported nonavailability of ARVs and forgetfulness as the major reasons for nonadherence to ART in children.[13] Furthermore, in contrast to our study, some studies from Nigeria identified drug stock-out, financial constraints, unavailability, and inaccessibility to medications as the most common reasons for nonadherence.[8,9] This may be due to the fact that their patients had to purchase the ARV drugs themselves, whereas currently in most centers including our own, the ARV drugs are given free to the patients. In a review of 13 studies on adherence to ART in Nigeria, the most prevalent barriers to patient adherence were the cost of therapy, medication side effects, nonavailability of ARV drugs, and the stigma of taking the drugs.[14] However, most of those studies were carried out in the era where patients had to purchase their drugs and also in adult patients. Our study is also consistent with some studies done in adults where forgetfulness and traveling were reported as the most frequent reasons for nonadherence.[15-17]

Caregivers' factors were the major contributors to poor adherence, as shown by our study. Caregivers' age <35 years is significantly associated with poor adherence. The reason behind this is not clear, but a study from Southeastern Nigeria related it to social pressure and low economic power as they are the ones likely to be economically disadvantaged and unmarried.[15]

The children cared for by caregivers other than their biological parents had poorer adherence when compared to those under the care of their biological parents. This may be because most of the parents are also on the ARVs and therefore know the importance of adherence. Studies from Brazil and Togo also reported that children who are being taking care of by people other than their biological parents are more likely not to adhere to their ARV drugs.[18,19] Other studies, however, showed that mothers being the caregiver are associated with poor adherence associating it with mothers' advanced disease and untreated psychological symptoms.[7,20] In our study, however, mothers that were positive are already on drugs and so are not very sick.

Educational level of caregiver was significantly associated with poor adherence. Children whose caregiver had at least primary education were three times less likely to be adherent. The reason for this is unclear in our study. However, this finding is consistent with findings from a study from Southeastern Nigeria by Uzochukwu *et al*.[15] which asserted that those with formal education are more likely to be aware of the side effects of ARV medications and so stop the drugs with slightest impression of the side effects and therefore are less likely to adhere to ARV medications. On the other hand, those without formal education would tend to respect the advice of the doctor and therefore be more likely to adhere to ARV medication.[21] A study from Brazil, however, found that increasing educational level of caregiver is a protective factor against nonadherence, with an apparent dose–response effect.[18] Studies from Brazil and Malawi also showed that there is a positive relationship

between increasing educational level and increasing adherence to ART.[18,22] Other studies, however, showed that level of education has no effect on adherence.[7,23]

Children whose caregivers are HIV positive and are on ART were more than twice as likely to adhere to their ART. This may be because the caregivers on ART may have better knowledge of the drugs and the importance of the adherence as they are also taking it. This finding is consistent with studies from Zambia and Mozambique that showed that having a partner such as a spouse, family member, or friend who is also on ARV medications improves adherence.[24,25] A study from Brazil also showed that a situation in which the caregiver was seropositive for HIV and is not under ARV treatment seemed to increase the child's risk of nonadherence.[18]

Our study showed no relationship between adherence to ART and sex or marital status of the caregiver. This is similar to most previous studies but in contrast to a study from Ethiopia which reported that children whose caregivers were married or divorced were more adherent when compared with those whose caregivers were single.[12]

Findings from our study showed that demographic characteristics of the children, such as sex and age, and clinical characteristics such as HIV disclosure, disease stage, and ART regimen or duration did not significantly affect adherence to ART in children. Other studies showed divergent views, and a study from Kano, Nigeria, showed a significant association between adherence with regiment type and duration of therapy.[26] Another study from Ethiopia showed that children who were not aware of their status and those with advanced disease were more likely to have poor adherence.[12]

Conclusion

A high nonadherence of 23.4% was found in our study, despite scale-up of ART in Nigeria is high. Caregiver factors were the main factors associated with poor adherence in children with HIV. We recommend regular adherence counseling at every visit with emphasis on the use of reminder methods to improve adherence.

Our study is limited by the fact that we evaluated adherence using self-report which is subjective and can be affected by recall bias. We did not correlate self-report adherence to more objective measures, such as viral load and CD4 counts, because of financial and laboratory inadequacies.

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Conflicts of interest

There are no conflicts of interest.

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