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The Predictors of Adherence to Antiretroviral Therapy among HIV Positive Children in Enugu State, Nigeria

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Abstract

Antiretroviral therapy(ART) has been used to reduce morbidity and mortality of the HIV positive patients. However, an excellent therapeutic outcome of CD4 count >500 cells/mm^3 with ART requires ≥ 95% adherence to therapy. The purpose of this study was to determine the factors associated with adherence to ARV among children in an ART programme. A retrospective study was conducted for four months between the periods of March to June 2018 in University of Nigeria Teaching Hospital, Ituku Ozalla, Enugu, Nigeria. The adherence was measured using pre-tested, structured self administered questionaire. Adherence was defined as no missed Antiretroviral dose in the previous three days of therapy. The effects of factors such as level of education, type of caregiver, duration on therapy, proper education of caregiver, method of passing information on drug dosage and side effects, continuing education and support from health professionals on adherence were tested. Adherence level of HIV positive children was 69 %. Factors such as level of education, type of caregiver, duration on therapy, proper education(benefits of treatment and adverse effects of drug), method of passing information on drug dose and side effects, continuing education and support from health professionals on adherence investigated were found not to relate statistically significantly with adherence to ART. Therapy adherence level of HIV positive children was sub optimal. The type of caregiver, physician's behavoir and other factors did not show significant relationship with adherence. Adherence to antiretroviral therapy(ART) is closely associated with viral suppression and prevent progression to AIDS and death.

Keywords: *Adherence, HIV, therapy, caregiver, Nigeria.*

Introduction

The estimated number of children living with HIV was around 1.8 million in 2017 on all over the world. The greatest proportion of the children (90 %) lived in sub Saharan Africa(1). Around 180,000 children were newly infected with HIV virus. In Nigeria, UNICEF estimated that 270,000 children under age of 14 years were living with HIV in 2016 (2). Globally, in 2017, 940,000 children under age 15 years were receiving antiretroviral therapy (ART). This means that about half of children under the age of 15 years living with HIV were receiving ART (51%)(3).

ART is the critical point development in the treatment of HIV. It was a breakthrough in the industrialized world, leading to the reduction of mortality and the improvement of quality of life of people living with HIV and AIDS (PLWHA). It transformed the disease into a chronic treatable condition for a significant proportion of PLWHA with access to this treatment [4]. International guidelines advise that immediate ART should be initiated once HIV infection is detected in any child under the age 5 years (5). Early diagnosis and treatment is critical for infants as seen in study done on ART and mortality among HIV-infected infants in South Africa which demonstrated 76% of reduction in mortality (6).

Adherence to HIV treatment regimen is defined as taking pills according to the posology, dosage regimen and method of administration prescribed and recommended in official protocol. Available data suggests that

patients must take and maintain a high level (95% and beyond) of antiretroviral drug doses to maintain suppression of viral replication ([7). Adherence requires dedication of both the child and caregivers to consistently follow pharmacological treatment recommendations [8]. Non-adherence is the most common reason for treatment failure, with potential risk to develop drug resistance through suboptimal viral suppression. Subsequent transmission of first-line ART-resistant HIV strains increases demand for second-line treatment often associated with poorer patient health outcomes and increasing healthcare costs (9).

Studying the determinants of non-adherence to ART among HIV-infected persons is an important clinical and public health goals in controlling HIV- epidemic (10). A lot of studies on correlates of adherence found that only a few determinants were consistently associated with non-adherence, including adverse drug effects, psychological distress, lack of social support structures and complexity of the ART regimens. Socio-demographic characteristics, substance abuse, depression, CD4 cell count, and patient–provider relationships were found to be consistently associated with non-adherence for adult in another research[11]. In a study done on HIV positive children in Tanzania, determinants of adherence were experiencing ARV drug side effects, stigmatisation, affording transportation fee to clinic.(12). Promoters of adherence included counselling and education interventions, memory aids, and active disclosure of status by people living with HIV (13). To maximize adherence to ARV drugs: it is important to explain drug side-effects and how to manage these side-effects to both caregivers and children (12).

In this study, level and predictors of adherence to ART therapy among children living with HIV in Enugu was investigated.

Materials and Methods

A retrospective study was conducted for four months between the periods of March to June 2018. The location of the study is Paediatrics HIV Unit at the University of Nigeria Teaching Hospital, Ituku Ozalla (UNTH) in Enugu State. Enugu State is in the South Eastern part of Nigeria. The study population were the children aged 2 to 15 years who have been tested and confirmed HIV positive and accessing the Paediatric HIV clinic for the ART. They were 142 in number.The following inclusion criteria were met: having an identifiable caregiver to administer medication, attending clinic appointments and resided in Enugu for at least 3 months**.**

Ethical Approval

The study was approved by the University of Nigeria Teaching Hospital Health Research Ethics Committee with opinion no NHREC/05/01/2005B-FWA00002458-1RB00002323.

All parents/guardians gave written informed consent for the care giver's participation.

Data Collection

This study was carried out among 84 HIV positive paediatric patients. A questionnaire was administered to caregivers during the visit to assess experience with giving medication and self-reported adherence. Majority of the children have been commenced on the combination therapy, Zidovudine (AZT), Lamivudine (3TC) and Efavirenz (EFV-children >10 kg or >3 years) or Nevirapine in University of Nigeria Teaching Hospital, Ituku Ozalla Enugu.

Clinical and socio-demographic characteristics namely the WHO clinical staging, CD4 count, duration on HIV infection,duration on ART, age ,weight and sex of the child were collected from record on standardized data collection forms filled by their clinicians. The current staging system for HIV infection in children was set up in 2005 and establishes on the staging system in place since 1987. The staging system also demands the presence of HIV infection: HIV antibody for children aged 18 months or more; virology or P24 antigen positive test if aged under 18 months. Clinical staging is classified into four stages. Each stage has its own symptoms (14) Also caregiver socio-demographic characteristics were elicited with the questionnaire. Regimen related variables such as dosing schedules and frequency, administration burden and complexity, side effects, history of hospitalization were also ascertained.

For the purpose of this study, children were retrospectively re-staged according to medical record information using the WHO-stage clinical classification (15).

Measurement of adherence

A standardized questionnaire was administered to each caregiver. The questionnaire was adapted from Paediatric AIDS Clinical Trials Group (PACTG) adherence questionnaires modules 1 and 2 (16) and assessed caregiver's ability to accurately describe the ART regimen, recall of missed doses in the past 3 days, difficulties experienced with giving medication and beliefs about ART. Based on reported missed doses, children were classified as not fully adherent (NFA) if ≥ 1 dose was missed in the previous 3 days. Interviews were conducted in the caregiver's local language especially for those who cannot understand English language.

Data analysis

The analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 16.The relationship of factors such as level of educaton to adherence was determmined using Chi Square at test level of 5 % significance.

Results

This study was carried out among 84 HIV positive paediatric patients who attended out-patient Paediatric clinic, University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu. The results are presented below.

A total number of 84 caregivers filled the questionaire. The age group of 31-40 years had the highest frequency (48.8%) and there were 71 females (84.5%). Most of them had Primary school education (88.2%). The caregivers that were married accounted for 57.1 %. They were predominantly Christians. Ninety seven percent were of Ibo ethnic group. The rest were Idoma from Benue State. Ibo is an ethnic group located in South East Nigeria. They speak Igbo language. Business and civil service are their major occupation. On the other hand Idoma is an ethnic group located in Benue state. Benue is situated in North Central Nigeria. Their major occupation is farming.

The highest number of children 18(21.4%) was found in the age group 120- 143 months. There was a slight preponderance of males 48 (57.1%) (Table 1). A total of 58 (69.0%) of the children adhered to their ARV treatment while 26 (31.0%) did not (Fig 1).

A total of 26 (31.0%) of the children missed their dose in the past three days. The highest frequency of missed dose was once in the past three days (46.2 %) (Table 2).

Foster parent (100.0%) recorded the highest caregiver that adhered to ART. The least adherence to drugs (44.4%) was recorded in the case where uncles were the caregivers (Table 3). Children that have received their therapy for less than 24 months had better adherence to drugs compared to those that have had their drugs for 24 or more months (Table 4).

Table 1. Demographic characteristics of children

	Demographic Characteristic	**Frequency (n = 84)**	**Percent**
Age Group (Months)	≤ 23	5	6.0
	24 – 47	11	13.1
	48 – 71	15	17.8
	72 – 95	12	14.3
	96 – 119	12	14.3
	120 – 143	18	21.4
	144 – 167	3	3.6
	≥ 168	8	9.5
SEX	Male	48	57.1
	Female	36	42.9

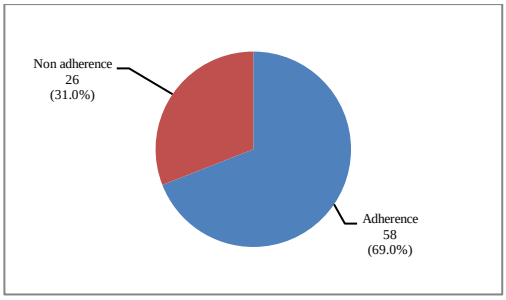

Figure 1. Adherence Rate to ART of HIV positive children

Table 2. Frequency of missed doses in the previous three days

Frequency	Number	Percent
Once	12	46.2
Twice	7	26.9
Thrice	3	11.5
Four times	4	15.4
Total	26	100.0

Table 3. Association between Adherence to ART and child's relationship to caregiver.

Category of Caregiver	Adherence		Total (%)
	Yes (%)	No (%)	
Parent	46 (73.0)	17 (27.0)	63 (100.0)
Uncle	4 (44.4)	5 (55.6)	9 (100.0)
Grandmother	3 (50.0)	3 (50.0)	6 (100.0)
Aunt	4 (80.0)	1 (20.0)	5 (100.0)
Foster parents	1 (100.0)	0 (0.0)	1 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi^2 = 4.761$, df = 4, p = 0.313 (Not statistically significant)

Table 4. Duration on therapy in relation to adherence to ART

Duration (Months)	Adherence		Total (%)
	Yes (%)	No (%)	
0 – 11	28 (66.7)	14 (33.3)	42 (100.0)
12 – 23	2 (100.0)	0 (0.0)	2 (100.0)
24 – 35	5 (55.6)	4 (44.4)	9 (100.0)
≥ 36	23 (74.2)	8 (25.8)	31 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi^2 = 2.159$, df = 3, p = 0.540 (Not statistically significant).

Education of caregiver association with adherence was not statistically significant (p = 0.240) (Table 5).

The behavior of doctor attending to the patient did not have any significant influence on their adherence to drugs. The least adherence 14 (66.7%) was noted in the patients whose doctors acted with enthusiasm and confidence (Table 6).

Out of a total of 70 caregivers that were properly educated (given information to patients on nature of disease and it's complication, benefits of the treatment and possible adverse effects of treatment) 49 (70.0%) adhered to their drugs(Table 7).

Table 5. Education of caregiver in relation to adherence to ART

Education	Adherence		Total (%)
	Yes (%)	No (%)	Total (%)
No formal education	6(75.9)	2 (25.0)	8 (100.0)
Primary education	12(52.2)	11 (47.8)	23 (100.0)
Secondary education	18 (69.2)	8 (30.8)	26 (100.0)
Tertiary education	20(80.0)	5 (20.0)	25 (100.0)
Others	2(100)	0 (0.0)	2 (100.0)
Total	58(69)	26 (31.0)	84 (100.0)

$\chi^2 = 5.497$, df = 4, p = 0.240 (Not statistically significant).

Table 6. Behavior of doctor attending to child in relation to adherence to ART

Behavior of Doctor	Adherence		Total (%)
	Yes (%)	No (%)	
Enthusiasm and confidence	14 (66.7)	7 (33.3)	21 (100.0)
Enthusiasm	38 (69.1)	17 (30.9)	55 (100.0)
No enthusiasm	6 (75.0)	2 (25.0)	8 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi 2 = 0.188$, df = 2, p = 0.910 (Not statistically significant).

Table 7. Proper education of caregiver on the nature of disease and implications of not taking drugs in relation to adherence to ART

Properly Educated	Adherence		Total (%)
	Yes (%)	No (%)	
Yes	49 (70.0)	21 (30.0)	70 (100.0)
No	9 (64.3)	5 (35.7)	14 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi 2 = 0.178$, df = 1, p = 0.673 (Not statistically significant)

Although adherence to drugs was higher 29 (72.5%) among the caregivers that did not receive regular education and support than those that received it(69%), the difference was not statistically significant (p = 0.514) (Table 8).

Adherence to drugs was better (70.7%) among the patients who had no stigmatization in their home environment (Table 9). However, there was no statistically significant difference when compared to those that were stigmatized.

WHO clinical stage of the children relates to adherence. The worst adherence to drugs (50.0%) was noted in the patients with advanced stage of HIV compared to the other stages(Table 10).

There was a general increase in weight of the children in both age groups at the end of the study, with more marked increase in the under five years old children (Table 11). However, these were not statistically significant.

Table 8. Regularity of education and support from health professionals in relation to adherence to ART

Regular Education and Support	Adherence		Total (%)
	Yes (%)	No (%)	
Yes	29 (65.9)	15 (34.1)	44 (100.0)
No	29 (72.5)	11 (27.5)	40 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi^2 = 0.426$, df = 1, p = 0.514 (Not statistically significant)

Table 9. Stigmatization in the home environment in relation to adherence to ART

Stigmatization	Adherence		Total (%)
	Yes (%)	No (%)	
Yes	5 (55.6)	4 (44.4)	9(100.0)
No	53 (70.7)	22 (29.3)	75 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi^2 = 0.859$, df = 1, p = 0.354 (Not statistically significant)

Table 10. WHO Paediatric staging of HIV/AIDS Disease in relation to adherence to ART [1]

WHO Stage	Adherence		Total (%)
	Yes (%)	No (%)	
1	20 (71.4)	8 (28.6)	28 (100.0)
2	21 (60.0)	14 (40.0)	35 (100.0)
3	15 (88.2)	2 (11.8)	17 (100.0)
4	2 (50.0)	2 (50.0)	4 (100.0)
Total	58 (69.0)	26 (31.0)	84 (100.0)

$\chi^2 = 5.022$, df = 3, p = 0.170 (Not statistically significant).

Table 11. Mean weight in relation to age of children

Age (Years)	Weight (Kg)		t-test	p-value
	Initial weight Mean±SD	Final weight Mean±SD		
< 5	13.61±3.77 (n = 24)	25.91±45.73 (n = 19)	1.32	0.195
≥ 5	27.41±7.47 (n = 57)	27.87±8.23 (n = 52)	0.31	0.760

Discussion

Adherence to drugs has been reported as an important criterion for improving the life of the HIV positive children(4,7). The level of adherence of the children was measured through self reporting. The level of adherence was 69% (63/84). This does not agree with a study which had 84% adherence by self assesses adherence (13).

Foster parent (100.0%) recorded the highest caregiver that adhered to ART .Type of caregiver had no significant relationship to adherence in this study. It is expected that parents should put eveything in place to ensure adherence after counselling. Poor adherence could be attributed to lack of commitment to therapy. The poor adherence to drugs when parents were care giver is in contrast to study done in USA as adult other than parents resulted in reduced adherence to ART (13).

Children that have received their therapy for less than 24 months had better adherence to drugs compared to those that have had their drugs for 24 or more months (Table 3). However, the difference was not statistically significant. It can be deduced that children who have taken drugs for more than 24 months must

have experienced side effects that resulted in poor adherence.

Literacy expressed as level of education factor was assessed. Education of caregiver association with adherence was not statistically significant. This is in line with cohort study carried out in USA (13). It was reported that education of caregiver has marginal effect on adherence. This findings was also similar to study conducted in Jamaica that level of education attained by care giver correlated with adherence to ART (19). Low level education of care givers was a significant risk factor for improper adherence to HIV medication regimens in the study investigated by Waite *et al* (20).

The behavoir of doctors including such things as enthusiasm, confidence, adequate time during consultation is expected to enhance adherence to ART. In this study least adherence was observed in patients whose doctors we're not enthusiasm. In contrast, a study done in Zambia shows that inadequate time during consultation affected the adherence (17). In another study pleasant attitude of health careprovider at the organization helped to enhance adherence (18).

Education on benefits of treatment and possible side effects communicated excellently did not significantly affect level of adherence to ART in this study. The care provider should be able to motivate caregiver by creating awareness and persuading them to accept the therapy and administer the drugs as instructed. Adherence to drugs was higher 29 (72.5%) among the caregivers that did not receive regular education and support than those that received it(69%). Regular education and support during each clinic visit ought to enhance and maintain good adherence.This result is contrary to the work conducted in Jamaica where the regular education and support had significant effect on the level on adherence (19).

Adherence to drugs was better (70.7%) among the patients who had no stigmatization in their home environment. Stigmatization in home environment had negative effect on adherence. Sigmatization was observed as an obstacle to wide disclosure of usage of ART thereby affecting adherence. This is in agreement with this study done in South Africa (21).

WHO clinical stage of the children relates to adherence. The worst adherence to drugs (50.0%) was noted in the patients with advanced stage of HIV compared to the other stages. It can be deduced that severity of disease had negative effect on adherence.

The general increase in weight of the children in both age groups (<5 and ≥ 5 years) inferred that there was a correlation between adherence and change in weight. Increased weight in <5 could be used to infer improved morbidity as a result of therapeutic outcome of adherence. Using weight as an indicator, marked increase in under 5 years means better adherence to ART.

Conclusion

This study found the level of adherence to be 69 % using self reporting measure. Adherence to ARV is challenging and are effected by several factors namely level of education, type of caregiver, duration of therapy, stigmatization, stage of sickness in the child, regularity of proper education and the presence of adverse effect. However, these factors had no statistical significance effect on adherence on HIV positive children attending clinic at UNTH in Enugu State.

Recommendation

It is recommended that adherence support workers be formed to maintain the effectiveness of ART by doing follow up visits to see if the patients are taking their medications correctly and also maintain a balanced diet. Caregivers should be encouraged to disclose the children's status and also inform responsible relation on . The disclosure will easily enable caregivers delegate administration of ART to HIV child when not available without fear of anticipated stigmatization.

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