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November 2017 Vol.:8, Issue:1

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Adherence to Antiretroviral Drugs among HIV Positive Adolescents at Comprehensive Care Clinic, Gertrude's Children Hospital, Nairobi, Kenya



IJSRM

INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY

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Submission: 19 October 2017

Accepted: 29 October 2017

Published: 30 November 2017



HUMAN JOURNALS

www.ijssrm.humanjournals.com

Keywords: Adherence, Antiretroviral Drugs, HIV Positive, Adolescents

ABSTRACT

Background; Antiretroviral treatment requires high-level (> 95%) adherence for optimal viral suppression. Published data on adherence to antiretroviral (ARVs) in Kenyan adolescents is very limited. The purpose of this study was to establish the prevalence of ARVs adherence among HIV positive adolescents at Comprehensive Care Centre, Gertrude's Children Hospital. **Methods;** This was a facility-based descriptive cross-sectional study, where 185 patients aged 10-18 years who had been on ARVs for at least two years were systematically and randomly selected. Among them, 129 respondents who were HIV fully disclosed were interviewed using a structured questionnaire about their experience taking ARVs. Adherence was measured based on a composite score derived from a three questions adherence tool developed by Center for Adherence Support Evaluation (CASE). Data was also collected from records retrieval. Data analysis was done using Epi data software 3.1 with statistical significance set at $p < 0.05$; Statistical analysis of Frequencies, correlations, ANOVA and multivariate logistic regression to test for predictors of adherence. **Results;** Overall, 185 patients were selected but 129 disclosed patients were interviewed; 52.7% males and 47.3% females, estimated level of adherence of 67.34% and the main (63.6%) reason for missing therapy was forgetting. Long waiting time in the clinic and stigmatization were other factors found to affect adherence. The CASE Index Tool depicted high reliability with a Cronbach's $\alpha = 0.696$. The results showed a significant positive correlation between CD4 counts and adherence ($R_h = 0.255$, $p = 0.003$) and a significant inverse correlation between Viral Load levels and Adherence ($R_h = -0.189$, $p = 0.031$). There was no significant association between HIV disclosure and ARVs adherence. **Conclusion and recommendations;** The 67.34% adherence level to ART reported in this study is below optimum adherence of 95%. This study gives the following recommendations; (a) Policy review on HIV disclosure procedures with training of health workers on it (b) Put fitting strategies to improve patients' ability to impact on forgetfulness (c) Clinic staff to adopt the use of CASE Tool in assessing adolescent's adherence to ARVs.

1. INTRODUCTION:

Globally the number of adolescents living with HIV is increasing rapidly. With improved access to care and treatment Young People Living with HIV (YPLHIV) irrespective of their mode of infection, are living longer and healthier lives [10, 41]. Sub-Saharan Africa accounts for almost 67% of all people living with HIV/AIDS [41] and yet only a handful of studies in the region have investigated outcomes on ART in the emerging group of HIV infected adolescents [4] sexually active contributed to increased rate of new HIV infections to their sexual partners; thus, young people aged 15–24 years accounted for 42% of new HIV infections in people aged 15 years and older; yet nearly 80% (4 million) of this YPLWHIV live in sub-Saharan Africa with Kenya being among the countries contributing to the highest burden [33].

In Kenya among the youth, HIV prevalence is higher among women than men. Between the age groups 15-19 years and 20-24 years, HIV prevalence among women nearly doubles, from 4% to 7 % [23]. Adolescents (ages 10–19) comprise about 25% of Kenya's total population and with its annual growth rate of 2.6%, Kenya's population is expected to more than double from approximately 39 million people in 2009 to 82 million people in 2035 thus too, will the population of youth in need of services [35]. Children who acquired HIV from their mothers are now living longer, healthier lives as a result of increased access to ARVs; these children comprise two groups of HIV infected adolescents; those who acquired HIV through vertical transmission and those who acquired HIV through horizontal transmission (largely sexual).

Adherence has been studied extensively in adult patients. However, issues in youth adherence and possible reasons for their poor adherence have received little attention in the literature [26]. 95% optimal adherence is required for viral inhibition [41]. The table below shows ARVS adherence in some selected studies with limited data in adolescents.

Table showing ARVs adherence levels from various studies across different places

In Kenya	In Africa / Intercontinental
Comparing the adherence level in several adolescents studies	
86%- Kisumu [16]	50%- United States of America (Murphy <i>et. al</i> , (2001) in [31]
Comparing adherence in the context of several adult studies	
48%- Nairobi, Kibera [9]	54%- Nigeria [12]
56.8%- Eldoret [32]	63%- South Africa [25]
64%- Mombasa [30]	21%- Tanzania [13]
74% -Nyeri [24]	76% -S. West Ethiopia [2]
72%- Nairobi [36]	78%- Cote D'Ivoire [8]
	87%- Cameroon [15]
	64%-Combined continental adherence [18] (55% in North America and 77% in Africa)

Antiretroviral therapy works to decrease viral loads hence improving quality of life [37]. Drug resistance brought about by poor or suboptimal adherence necessitates second-line drug treatment which can be more difficult to administer and the cost implications much higher and consumes the limited resources available for HIV programs [11,42]. Adherence to ART is an essential and life-long practice for the maintenance of health and longevity.

Despite the gains made in the fight against HIV, the dynamic nature of the epidemic continues to pose challenges to the medical field yet limited studies have been done in Africa on adolescents with HIV in issues relating to ART adherence. Studies have shown dramatically high virologic failure rates among adolescents [5, 22] yet optimal adherence of more than 95% to ARVs is critical to successful outcome of patients receiving therapy [39]. The consequences of poor adherence are failure of viral suppression, decrease CD4 cell count, disease progression, drug resistance, risk of transmission of resistant virus and limited future treatment options [27]. Issues particularly raising concern for adolescents living with HIV are three intertwined challenges: disclosure, adherence to antiretroviral therapy (ART), and the prevention of HIV transmission to sexual partners [37].

Measuring adherence can be difficult. There is “no Gold Standard” method of measuring adherence [6]. No single method is 100% effective. Currently used methods of assessing adherence include, client self report, observing clinic appointments, electronic monitoring devices, pill counts, provider estimation and measurement of medications in the bloodstream/

biological markers. Although self report tends to overestimate adherence, several studies have found that self report correlates fairly well with actual medication intake. One such method of client self report is use of CASE Adherence Tool [14]. The researchers found that this tool was able to predict virologic response and was highly correlated with the previously validated American Aids Clinical Trial Group (AACTG) three-day recall. The CASE Adherence Index is brief, not dependent on specific medication recall and requires limited training before it can be implemented in the field by both HIV practitioners and researchers.

There are very limited published studies regarding adherence to ARVs in HIV positive adolescents in Kenya [31] conducted a systematic review and meta-analysis of published studies globally on adherence to antiretroviral for adolescents living with HIV found a range of 28-69.8%. A study was done in Kisumu, Kenya by [16] on adolescents adherence to antiretroviral and cotrimoxazole preventive therapy found adherence of 86%.

Gertrude's Children's Hospital is the only wholly pediatric hospital in East and Central Africa, which is a private and not for profit making institution situated in the outskirts Nairobi County. In addition, the hospital has ten satellite branches within and outside Nairobi. This institution is currently the main regional centre (East & Central Africa) in capacity building for Health Care Workers, in best practice in Pediatric HIV Management Courses including Trainer of Trainees Courses. The Comprehensive Care Centre (CCC), is an outpatient clinic that cares for HIV positive children from birth through adolescence until transition to adult care setups. The clinic also takes care of adults especially families of index pediatric cases. Since its existence in the year 2001, the clinic has had upward trends in patients' enrollment each year with current number of about 1100 adolescents (10-19 years) attending this clinic. The clinic is supported by organizations such as Presidents Emergency Plan for AIDS Relief (PEPFAR), Ministry of Health and National Aids & STIS Control Programme. Staffs in the clinic also do home visits to selected patients with complex family situations especially when related to adherence issues.

Patient defaulter has been increasing steadily in teenage years compared to later years when the adolescents are still in the care of their parents/guardians. There is no single study that has been carried out at the CCC on adherence to ARVS in adolescents. This study will seek to bridge this literature gap and hence provide concrete information to spearhead ARVs adherence issues in adolescents attending Gertrude's Children Hospital, Nairobi. Knowledge of the adherence levels will influence interventions aimed at decreasing cases of patient

defaulter. Policymakers and program planners will utilize this information to develop policies that enhance ARVs adherences as well mobilize resources needed appropriately.

2. Setting and target population

This was a facility based descriptive cross-sectional study. Both quantitative and qualitative data were gathered. The study area was Gertrude's Children's Hospital and the setting was the Comprehensive Care Centre located in the main hospital. This hospital is the only wholly pediatric hospital in East and Central Africa. The study population included all HIV positive adolescents (10-18 years of age) who were on ART and were enlisted in the Comprehensive Care Database. Eligible patients were sampled from the main hospital database only because the satellite clinics do not attend the HIV patients. By the age of 14 years majority (approx 80%) have full disclosure of their HIV status; the remaining (approx 20%) have partial disclosure.

The sample size was determined based on a prevalence of adherence study done in Kisumu, which showed an average adherence of 86% to ART among HIV positive adolescents [16]. Study participants were selected using systemic sampling whereby a list of all actively followed HIV positive adolescents with return dates within the study period was obtained from the patient's records (electronic database). Desired sample size of 185 patients was obtained using a predetermined interval. The selected subjects were then interviewed as they revisited the facility.

The inclusion criteria was that HIV positive male and female adolescents aged between 10 to 18 years who were accompanied by their parents/guardians to the clinic and had been taking ART for at least two years (active patients). The study excluded adolescents who were mentally handicapped and not capable of verbally communicating because they were not able to offer quality information required and those who were not fully disclosed to prevent accidental disclosure. Data was collected via interviewer-administered structured questions, CASE Index tool and Patient Medical Record Tool. The questionnaire sought information on socio-demographic, knowledge on ART and its side effects and reasons for missing appointments. Patient medical tool sought information regarding clinical markers of CD4, viral loads and level of disclosure (fully or partial).

Data collected was inspected, cleaned, coded and then analyzed using Epi data software 3.1 with statistical significance set at $p < 0.05$. Descriptive statistical tests (mean, median, and

standard deviation) were used. Ethical considerations included seeking approval to carry out research from the Institutional Research and Ethics Committee (IREC) of Moi University and IREC committee of Gertrude’s Children Hospital. Informed consent in form of writing was obtained from all study participants who were accompanied by parents/guardians which clearly explained to participants what the study was investigating. Confidentiality and privacy were guaranteed to the participants by explaining to them any information obtained from them would be treated with utmost confidence and that privacy would be ensured during the session(s). That any information about the participant would have a number instead of a name thus ensuring anonymity. Autonomy was guaranteed with participants allowed to be engaged in the study at their own free will. They were allowed to withdraw in the course of the study if they so wish.

3. RESULTS

3.1 Social demographic characteristics of respondents

Baseline variables	Categories	Frequency (n=129)	Percentage (%)
Gender	Male	68	52.7
	Female	61	47.3
Education level	No formal education	2	1.6
	Primary	38	29.5
	Secondary	77	59.7
	Tertiary	12	9.3
Occupation	Employed	11	8.5
	Unemployed	2	1.6
	Student	116	89.9
Religion	Christians	125	96.9
	Muslims	4	3.1
Age	10-12yrs	9	7.0
	13-15yrs	56	43.4
	16-18yrs	64	49.6
	Mean (SD)	15.3 (1.8)	
	Median (Range)	15 (11-18)	
Place of living	Urban(within Nairobi)	91	70.5
	Rural(outside Nairobi)	38	29.5
Whom living with	Parents	64	49.6
	Relatives	21	16.3
	Friends	9	7.0
	Siblings	13	10.1
	Others	22	17.1

3.2 Clinical details of respondents (n = 129) and (n =185) **

Baseline variables	Categories	Frequency (n=129)	Percentage (%)
HIV status disclosure **	Disclosed	129	69.7
	Not disclosed	56	30.3
Latest CD ₄ count	Below 500	44	34.1
	Above 500	85	65.9
	Mean (SD)	636.3 (258.1)	
	Median (Range)	621 (25-1236)	
	Latest Viral loads	Undetectable (<40copies/ml)	67
	Below 1000	28	21.7
	Above 1000	34	26.4
	Mean (SD)	49904.6 (295123.9)	
	Median (Range)	40 (40 - 3151438)	
Duration ARVs taken	2-5years	70	54.3
	6-10years	54	41.9
	Over 11years	5	3.9
	Mean (SD)	5.6 (2.6)	
	Median (Range)	5 (2-13)	

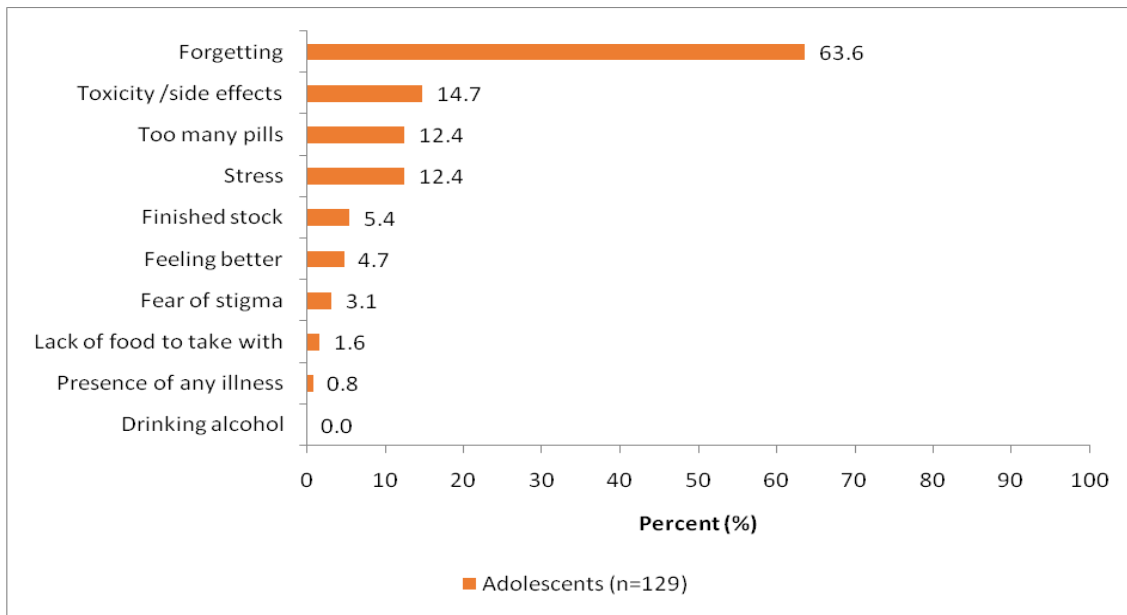
3.3 Estimated level of adherence

Adolescent’s adherence level was measured by CASE Index Tool, consisting three set of questions and their responses and whose scores were summed up to obtain a composite score that ranged from 3 to 16 points. Their total values were then converted to percentages. The mean ARVS Adherence level was 67.3%.

Variable	N	Mean	Median	SD	Min	Max	Range	Skewness	Kurtosis
CASE Index Tool (% Adherence levels)	129	67.3	68.7	18.2	25.0	100.0	75.0	-0.13	-0.82

3.4 Reasons given for missing drugs

Forgetting was the leading reason for missing doses (63.6%) seconded by toxicity/side effects of meds (14.7%), and thirdly stress and too many pills (12.4%) each.



3.5 Relationship between social demographic characteristics and ARV adherence

The results from a two-sample independent t-test in the table below showed that adherence level is equally distributed across all the social demographic characteristics.

Baseline variables	Categories	N = (129)	Mean Adherence (%)	Standard Deviation	T-test Anova* p-values
Gender	Male	68	67.7	18.6	0.7960
	Female	61	66.9	17.9	
Education level	No formal education	2	59.4	13.3	0.4889
	Primary	38	67.6	18.2	
	Secondary	77	68.5	18.1	
	Tertiary	12	60.4	19.1	
Occupation	Employed	11	60.8	19.4	0.4212
	Unemployed	2	62.5	17.7	
	Student	116	68.0	18.1	
Religion	Christians	125	67.4	18.4	0.8484
	Muslims	4	65.6	13.0	
Age *	10-12 yrs	9	71.5	17.1	0.7305
	13-15 yrs	56	66.4	19.1	
	16-18 yrs	64	67.6	17.7	
Place of living	Urban (within Nairobi)	91	67.2	18.4	0.8667
	Rural (outside Nairobi)	38	67.8	17.9	
Whom living with	Parents	64	65.9	18.7	0.5134
	Relatives	21	63.7	15.5	
	Friends	9	71.5	18.8	
	Siblings	13	69.7	19.9	
	Others	22	71.9	18.0	

* T-test was used to assess differences where there were only two levels of the categorical variable while ANOVA was used where there were more than two levels.

3.6 Pearson Correlation Matrix between adherence levels and clinical lab markers

The results showed a significant positive correlation between CD₄ count levels and Adherence level ($Rho=0.255, p=0.003$) and a significant but negative correlation between Viral Load levels and adherence level ($Rho= -0.189, p=0.031$).

Pearson Correlation Coefficients Matrix for HIV disclosed adolescents

Pearson Correlation Coefficients, N = 129 Prob > r under H0: Rho=0				
	CD ₄ Counts	Viral Load	Duration on ARV	Adherence Level
Latest CD ₄ Counts	1.000	-0.160 0.069	0.108 0.221	0.255* 0.003
Latest Viral Load s	-0.160 0.069	1.000	-0.117 0.184	-0.189* 0.031
Duration on ARVs:	0.108 0.222	-0.117 0.184	1.000	0.028 0.748
Adherence Level	0.255* 0.003	-0.189* 0.031	0.028 0.748	1.000

*Pearson Correlation Coefficient statistically significant at 5% level of significance.

4. DISCUSSION

ARVS adherence levels: There exists limited published data supporting ARVs adherence in Kenya among HIV positive adolescents and therefore this discussion will bring on board some studies done on adult ART adherence studies in Kenya, Africa and other developing countries. This adherence could be attributed to the fact most respondents were 15 years old, majority lived with their parents hence influence from parental supervision and also from the higher rate of HIV disclosure (WHO, 2004). Another argument for improved adherence is the broad diversity in the provision of various health services from one facility to another for the patients.

The level of adherence to ARVs was equal in all the socio-demographic characteristics. This finding was consistent with a study done by [1] who did not find any association between adherence to ART with sex, age and education levels. Possible reason for this could be the fact that majority of the respondents had a similar demographic characteristic that is 15years old and living with their parents hence influences from parents/guardians.

The results denoting significant positive correlation between CD₄ counts and adherence ($Rho=0.255$, $p=0.003$) and a significant inverse correlation between Viral Load levels and Adherence level ($Rho= -0.189$, $p=0.031$) means an increase in CD₄ count was associated with better adherence level and hence a decrease in viral loads. The lower the adherence level the higher the viral loads and the lesser the CD₄ counts. Adherence to ART was, therefore, found to be a predictor of laboratory markers/clinical outcomes (the viral load and CD₄ count). This agrees with literature by [37] who reported that HIV infection leads to disruption of specific T lymphocytes that bear the CD4 receptor. ART works to decrease viral loads hence improving quality of life.

Predictors of ARV adherence:

Demographic factors; None had significant influence. This finding differs from a study done by [20] who found that the younger age group was associated with poorer adherence while in other studies there was found no association on either adherence or non-adherence [7, 19] [38] in their study on predictors of adherence to ART in children and adolescents with HIV infection found the poorest adherence to be in the older adolescents aged 15 to 18 years. In addition, [38] found that female subjects and those without English as their primary language had marginally significant increases in the odds of non-adherence. School attendance was associated with better adherence in a longitudinal ART adherence study in adolescents living with HIV while unstable household was associated with poorer adherence [17, 20]. This can be argued that most of the respondents had more similar social demographic characteristics with mean age 15 years. *Medication factors:* Forgetting (63.6%) was a leading cause of missing doses which can contribute to poor adherence to ARVs. This finding was similar to a study done in Uganda [21], where the most cited reason for missing doses was forgetting (32%). Forgetting was also cited as a factor influencing adherence in an Indian study by [29]. In addition, toxicity /side effect (14.7%) was also found in a study by [19, 20] where adverse medication effects were associated with poor adherence. Too many pills and stress were causes of missed pills thereby influencing adherence to ARVs. In a study by [19, 20], a low pill burden was associated with improved adherence. The insignificance between the number of years one had been on ARVs and adherence levels ($r=0.028$, $p=0.0748$) differs considerably with those obtained by [3] who found that long duration of ART therapy was associated with pill fatigue and therefore poor adherence especially in the perinatally infected adolescents who may have started treatment early on in life.

5. CONCLUSION

The 67% ARV adherence level reported in this study is below optimum adherence of 95% that is necessary for inhibition of viral replication. The main reason cited affecting medication intake was forgetting and clinic long waiting time even though pill fatigue and side effects also had a significant attribute. The CASE Index tool yielded consistency in its use for the first time in adolescent population.

Recommendation: Since ARVs are vital in improving mortality and morbidity among HIV infected patients, it is now free in many centers in Kenya. Efforts should address barriers to uptake of ARVS. The researcher gives the following recommendations:

- Policy review about HIV disclosure guidelines and procedures with further training of health workers on them
- Facility staff to put fitting strategies to improve patients' ability to impact on forgetfulness and long waiting time
- Clinic staff to adopt the use of CASE Tool in assessing adolescent's adherence to ARVs
- Future research to examine other covariates to HIV disclosure that were not included in the model which have significant relationship on adherence

ACKNOWLEDGEMENT

We sincerely thank all the adolescents who voluntarily participated in this study plus the Health Managers of Gertrudes Children Hospital, for allowing this research to be conducted in the health facilities and permission to publish these findings. More appreciations go Dr. Penina Masibo, and Mr. Leonard Otieno for their support, encouragement and guidance during the study. Lastly, we are grateful to all those people who helped us either directly or indirectly to make this study a success.

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