Review Article

Determinants of Adherence to Antiretroviral Among HIV Positive Adolescents at Comprehensive Care Clinic, Gertrude's Children Hospital, Nairobi, Kenya

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Abstract: Antiretroviral drugs (ARVs) requires adherence of more than 95% for adequate viral suppression. The consequences of poor adherence are failure of viral suppression, decrease CD_4 cell count, disease progression, drug resistance, risk of transmission of resistance virus and limited future treatment options. Published data on adherence to ARVs in Kenyan adolescents is limited. The purpose of this study was to determine the ARVS adherence level and describe the healthcare system, medication and social environmental factors affecting this adherence among Human Immune-deficiency Virus (HIV) positive adolescents. This was a 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. Only 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 via Focused Group Discussion, Key Informant Interviews and from records retrieval. Data analysis was done using Epi data software 3.1 with statistical significance set at p<0.05. 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 α=0.696. The results showed a significant positive correlation between CD_4 counts and adherence (Rh0=0.255, p=0.003) and a significant inverse correlation between Viral Load levels and Adherence (Rh0= -0.189, p=0.031). Therefore, 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.

Keywords: HIV Infected Adolescents, Comprehensive Care Clinic, Adherence to ARVs

1. Introduction

Children who acquired HIV from their mothers comprise two groups of HIV infected adolescents who are now living longer, healthier lives as a result of increased access to antiretroviral therapy; those who acquired HIV through

vertical transmission and those who acquired HIV through horizontal transmission (largely sexual). Globally the number of adolescents living with HIV is increasing rapidly. It is estimated that 10.3 million youth aged 15-24 years are living with HIV/Acquired Immune-Deficiency Syndrome, AIDS (most without knowing that they are infected) and half of all new infections are occurring among young people on a global basis [49]. 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 [13, 48].

Sub-Saharan Africa accounts for almost 67% of all people living with HIV/AIDS [48] 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 [42].

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% [31]. 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 [43]. The question to ponder about this is, "What will be the implication of this statistics for a HIV infected generation by then"?

Adherence has been studied extensively with adult patients. However, issues in youth adherence and possible reasons for their poor adherence have received little attention in the literature [35]. 95% optimal adherence is required for viral inhibition [48]. The table below shows ARVS adherence in some selected studies with limited data in adolescents.

Table 1. 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 [21]	50%- United States of America (Murphy *et. al,* (2001) in [40]
Comparing adherence in the context of several adult studies	
48%- Nairobi, Kibera [12]	54%- Nigeria [17]
56.8%- Eldoret [41]	63%- South Africa [33]
64%- Mombasa [39]	21%- Tanzania [18]
74% -Nyeri [32]	76% -South West Ethiopia [1]
72%- Nairobi [49]	78%- Cote D'Ivore [11]
	87%- Cameroon [20]
	64%-Combined continental adherence [24] (55% in North America and 77% in Africa)

Measuring adherence can be difficult because there is "no Gold Standard" method of measuring adherence [7]. 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 blood stream/ 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 [19]. 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 tool 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.

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 especially in issues relating to factors affecting ARVs adherence. Studies have shown dramatically high virologic failure rates among adolescents [6, 29] yet optimal adherence of more than 95% to ARVs is critical to successful outcome of patients receiving therapy [47]. Drug resistance brought about by poor or sub optimal 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 [16, 50]. As a result, the consequences of poor adherence are failure of viral suppression, decrease CD_4 cell count, disease progression, drug resistance, risk of transmission of resistance virus and limited future treatment options [36]. Possible factors that influence adherence in adolescents are;

Demographic factors: Demographic factors such as age and gender described in literature have been inconsistent in predicting adherence in adolescents [27]. The younger age group was associated with poorer adherence while in other studies there was found no association either adherence or non-adherence [8, 26]. In a study on predictors of adherence to ART in children and adolescents with HIV infection found the worst adherence to be in the older adolescents aged 15 to 18 years [46]. Gender has not been shown to be a major demographic factor that influences adherence in the same study. The researchers found that female subjects and those without English as their primary language had marginally significant increases in the odds of non-adherence [46]. 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 [22, 27]. Some of these factors may be targeted in

intervention strategies.

Psychosocial factors: Several studies have identified a number of psychosocial factors associated with poor adherence and non-adherence to ART including HIV stigma, discrimination by friends and family members, depression, nondisclosure of HIV status, low levels of literacy, impact of long-term treatment on lifestyle as well as interference with school activities [3, 5, 9, 34, 37]. Researchers in Botswana investigated challenges faced by adolescents living with HIV and found that stigma, discrimination, HIV disclosure are associated with treatment adherence [34]. In a cross-sectional study of youth perinatally infected with HIV, no significant differences in the frequency of mental health disorders were found between adherent and non-adherent participants [38]. A review of published papers on adherence among HIV-infected youth, however, suggests that depression and anxiety have been consistently associated with poorer adherence [38].

Social support: In a review of literature on HIV antiretroviral adherence and intervention studies among HIV-positive youth conducted, there was no association found between social support and adherence to ART [37]. Stigma and discrimination by friends and family members were strongly associated with non-adherence to ART. However lack of family and social support was listed least as one of the adherence concerns in adolescents. Some researchers had an interesting finding from a past study; the association of adherence with presence of a biological parent as opposed to any type of a caregiver [46]. There are many orphaned children as a result of the mortality associated with HIV but it looks like that in the event of a biological parent being present, it is not protective. The presence of another adult caregiver who is not the biological parent seems to be protective for non-adherence [46].

Patient-provider relationship: In some study, researchers found good patient-provider relationship and patients' satisfaction with health care services have shown positive correlation with adherence to ART in some settings, however regular contact with either counselors or time spend with providers were not associated with adherence [25, 45].

Medication related factors: Regimen fatigue also has been identified as a barrier to adherence in adolescents [23]. Several studies have identified pill burden as well as lifestyle issues as barriers to complete adherence [14, 26]. Medication factors such as inconvenient dosing frequency, complex regimens, difficulty taking medications, dietary restrictions, pill burden, and lack of belief in the effectiveness of medication and side effects of ART affect adherence [7]. A low pill burden was associated with improved adherence while both physical and psychological medication-related adverse effects were associated with poor adherence [26, 27]. Others showed that the longer the duration of taking ART the poorer the adherence due to pill fatigue especially in perinatally infected adolescents who may have started treatment early on in life [3, 7].

Other factors: Alcohol or substance abuse, poor school attendance, and advanced HIV disease all correlated with non-adherence in a study conducted by [27, 37]. HIV disclosure is expected to eventually improve adherence, this

was found to be true in the same study conducted in Botswana on adolescents' adherence to ART. Non-disclosure of HIV status was associated with poor adherence to ART [3, 5, 10, and 34].

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 adolescents until transition to adult care set ups. 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 & Sexually Transmitted Infections 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 teen age 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 factors influencing ARVS adherence will revamp interventions aimed at decreasing cases of patient defaulter. Policy makers and program planners will utilize this information to develop policies that enhance ARVs adherences as well mobilize resources needed appropriately.

2. Methods

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. 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 patients records (electronic database). Desired sample size of 185 patients was obtained using a predetermined interval and the selected subjects were then interviewed as they revisited the facility.

The inclusion criteria was those 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 (allowed to recruit the active patients). The study excluded adolescents who were mentally handicapped and not capable of verbally communicating 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, Focused Group Discussion and from Key Informant Interview with two HCWs in the clinic. Data collected was inspected, cleaned, coded and then analyzed using Epi data software 3.1 with statistical significance set at p<0.05. 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 was 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

Table 2. Showing the 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
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

*Table 3. Showing the 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 (<40 copies/ml)	67	51.9
	Below 1000	28	21.7
	Above 1000	34	26.4
	Mean (SD)	49904.6 (295123.9)	
	Median (Range)	40 (40 - 3151438)	
Duration ARVs taken	2-5 years	70	54.3
	6-10 years	54	41.9
	Over 11 years	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%.

3.4. Factors Influencing ARVS Adherence

3.4.1. Medication Factors

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.
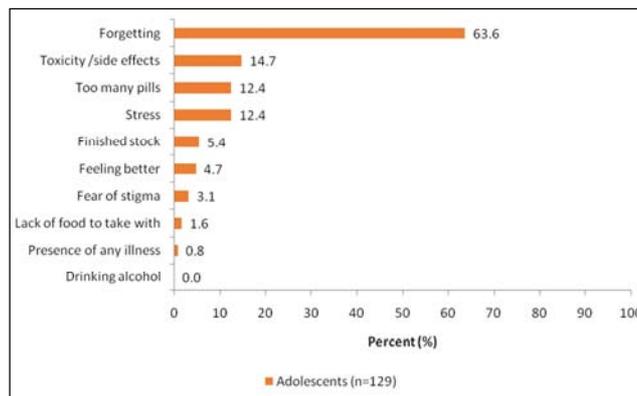

Figure 1. *Showing side effect experienced on taking ARVs.*

3.4.2. Health Care Factors as Rated by Respondents

Table 4. *Showing rating of healthcare factors.*

	Rating		
	Disagree	Neutral	Agree
Health care Factors	**%**	**%**	**%**
Confidentiality and privacy is maintained	0	1.6	98.4
HCW give plenty of information	2.3	6.2	91.5
HCW are friendly to patients	0	0	100.0
I trust health workers	2.3	7.0	90.7
Services are costly	87.6	6.2	6.2
The clinic has long waiting time	41.1	10.1	48.8
The clinic is located too far from town	65.9	12.4	21.7
The clinic makes call/send SMS reminder for revisit	4.7	3.1	92.2
There is provision of quality care	1.6	0.8	97.6

4. Discussion

a) Demographic factors: None had significant influence. This finding differs a group of researchers who found that the younger age group was associated with poorer adherence [27] while in other studies there was found no association on either adherence or non-adherence [8, 26]. Another 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 [46]. In addition, the researchers found that female subjects and those without English as their primary language had marginally significant increases in the odds of non-adherence [46]. 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 [22, 27]. This can be argued that most of the respondents had more similar social demographic characteristics with mean age 15 years.

b) HIV disclosure: The prevalence of HIV status disclosure was 69%. In several studies where HIV disclosure was low, they were found to have low ART adherence. In Botswana, for example, the challenges faced by adolescents living with HIV were investigated and found to be stigma, discrimination and HIV disclosure- all associated with treatment adherence. In resource-limited settings, disclosure of HIV status has been identified as a factor strongly associated with better adherence [15] and ultimately higher retention in care [2]. Another study by Reddington also showed that children whose HIV status was not disclosed had lower adherence levels [36]. This adherence level can be attributed to increased rate of HIV disclosure level even though the timing of HIV diagnosis is not known.

c) Medication factors: Forgetting was a leading cause of missing doses contributing to poor adherence to ARVs. Another study in Uganda and in India had this similar finding [28, 39]. Second were toxicity /side effect where adverse medication effects were associated with poor adherence [26, 27]. Too many pills and stress were causes of missed pills thereby influencing adherence to ARVs. In the same studies low pill burden was associated with improved adherence [26, 27]. In a study on psychosocial factors affecting medication adherence among HIV-1 infected adults receiving combination antiretroviral therapy in Botswana, the researchers found depression was associated with poor adherence rates [9]. The insignificance between the number of years one had been on ARVs and adherence levels (r=0.028, p=0.0748) differed considerably with some studies [3, 7]. The researchers 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.

d) Healthcare related factors such as clinic having a long

waiting time as indicated by results in this study (48.8%) can influence clinic appointments/ revisits for pill refill, hence becoming a factor leading to poor adherence. For instance, long waiting ques in the facility was a predictor for poor ART adherence in Tanzania [18].

e) Social/environmental factors: No effect of social support on adherence. This is different with findings of a study in South Africa where it was found that social barriers to adherence included lack of family support and fear of stigma [1]. The results also agree with a study conducted on HIV antiretroviral adherence and intervention studies among HIV-positive youth and who found no association between social support and ART adherence [37].

f) Other factors: From adolescents FGD the barriers which were stated to affect HIV status disclosure were fear of rejection/isolation, discrimination and stigmatization [37]. In-depth interviews with adolescents living with HIV aged between 10 and 20 years and their caregivers at six different AIDS treatment centers in Sao Paulo, Brazil also identified stigma and discrimination as the challenges in living with HIV [3].

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.

Recommendations: 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:

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

Acknowledgements

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