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FACTORS INFLUENCING ANTI-RETROVIRAL DRUG ADHERENCE IN HIV INFECTED CHILDREN ATTENDING KERICHO DISTRICT HOSPITAL, KENYA

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ABSTRACT

Objective: **To identify factors influencing anti-retroviral (ARV) drug adherence by HIV infected children aged 3 to 14 years attending Kericho District Hospital (KDH), Kenya.**
Design: **A cross-sectional study**
Setting: **Kericho District Hospital, Kenya**
Subjects: **Two hundred and thirty (230) HIV infected children aged 3 to 14 years under caregivers who had been on ARV treatment for at least three months before study as verified by clinicians.**
Results: **A total of 230 children aged between 3 and 14 years (mean age was 8.5 years ±3.2SD) were enrolled. Caregivers were aged between 16 and 90 years (mean age 34.6 years ± 10.4 SD). Majority, 178 (77.4%), of the caregivers were female and 137 (59.6%) were biological parents.   ARV drug adherence levels, based on various methods of assessment, were sub-optimum, varied from 56.1% based on time of taking drugs, 49.1% based on pharmacy drug refills, 45.7% based on clinic appointments to 27.0% by pill counts.The key factors associated with adherence based on time of taking drugs were: caregiver being away from home (p=0.0010), caregiver forgetting to give drugs to the child (p=0.020), lack of disclosure of the child's HIV infection status (p=0.0080) and side effects experienced by the child (p=0.0120), lack of knowledge on treatment (p=0.0030) and stigma (p=0.0470). Based on clinic appointments, the factors included caregiver being away from home (p=0.004), lack of disclosure of the child's HIV infection (p=0.0000), side effects experienced by the child (p= 0.0030), stigma (p=0.0070) and transport cost (p=0.0240).**
Conclusion: **The most important adherence factors among children were: caregiver being away from home, caregiver forgetting, lack of disclosure, child experiencing side effects, lack of knowledge and skills in managing the disease, stigma and transport costs to hospital.**

INTRODUCTION

There are an estimated 2.3 million children under the age of 15 with HIV / AIDS worldwide, 1.8 million of them in sub Saharan-Africa (1), and 330,000 children died of AIDS in 2007 (2). While the number of adults on anti-retroviral therapy (ART) has significantly increased in the last few years, the treatment of children still lags behind. Without access to ART, about 50.0% of children infected with HIV at birth die by their second birthday (3). In Kenya, 184,052 children were infected with HIV in 2009. Of these, 28,370 were on anti-retroviral treatment, covering about 24.2% of

children in need of anti-retroviral treatment (4). Anti-retroviral (ARV) drugs are effective in suppressing HIV replication; decreasing morbidity and mortality associated with HIV and improving quality of life in both adults and children infected with HIV (5) but drugs don't work in patients who don't take them as prescribed. Optimum drug adherence of more than 95% is critical for effective suppression of HIV infection (6). Adherence to ARVs remains a major challenge particularly in children, and several studies suggest that it is sub-optimal (2,7,9). It has been shown that missing even only one tablet in a week translates to 92.8% adherence (6). All potential

barriers to medication therefore need to be identified and appropriate measures developed to improve adherence (8). In Kenya, factors affecting ARV drug adherence in children are not well understood, and no comprehensive studies have so far been done to identify factors that influence adherence. Little information is currently available on strategies to improve adherence in HIV-infected children. This study therefore sought to examine factors affecting ARV drug adherence by HIV infected children seeking treatment at Kericho District Hospital in Kenya.

MATERIALS AND METHODS

Study area and study design: A cross-sectional study was conducted at Kericho District Hospital (KDH), located in South Rift Valley Province, Kenya, between August 2010 and January 2011. The hospital with a bed capacity of 250 offers comprehensive HIV prevention, care and treatment services supported by the President's Emergency Plan For AIDS Relief (PEPFAR) Programme. It also has established HIV/AIDS Electronic Medical Record system (EMR). By 2010 KDH had enrolled over 1000 HIV-infected children, of these 535 were on ARVs while 500 were on care support and not taking ARVs.

Study population: The study population comprised HIV infected children aged between 3 and 14 years who had been on ARVs for at least three months before the study and who were on follow up at KDH. The investigators working in collaboration with the clinicians enrolled the children. A caregiver was eligible if the child had a confirmed diagnosis of HIV infection and had been on ARVs for at least three months before the study; and the caregiver was a biological parent, relative, adoptive guardian, grandparent or an older sibling above 18 years.

Data collection: Before embarking on data collection, the research proposal was reviewed and approval to carry out this study was sought from Institutional Research and Ethical Committee (IREC) of Moi University and Moi Teaching and Referral Hospital, Eldoret, Kenya. IREC then notified the National Council of Science and Technology (NCST) of the approval of the study. Two research assistants (one clinical officer and a nurse) who worked in the HAART clinic were trained on data collection. Interviewers including clinicians were trained by the principal investigator on administration of and standardisation of the questionnaire for accuracy and comparability of the responses. Structured pre-tested, interviewer-administered questionnaire was used for data collection from caregivers. Data collection was carried out for six months from August 2010 to January 2011. The overall activity was monitored by the principal investigator.

The content of the questionnaire included: Socio-demographic variables such as child and caregiver gender, age, education, caregiver relationship to the child (biological or adoptive parent, grandparent, sibling or other relatives). The other demographic information of the caregivers included; education status, socio-economic factors (employment status, health insurance/financial support to the child,) and marital status of caregiver. Interviewer-administered questionnaire was administered to caregivers to determine demographic characteristics of the children and caregivers. Caregivers whose children were not adhering to ARV drug adherence based on time of taking drugs and clinic appointments were further interviewed to determine perceived determinants of drug adherence. Adherence factors based on pill counts and pharmacy refills were not determined as adherence levels were obtained from clinicians summary who did pill counting and pharmacy records respectively.

Data analysis: Descriptive analysis of demographics and adherence factors was done using Statistical Package for Social Sciences (SPSS) version 12.0.1 while logistic regression analysis using STATA statistical software was used to identify the most important factors influencing adherence. The level of statistical significance was set $p < 0.05$.

Ethical clearance: The study was reviewed and approved by Institutional Research and Ethics Committee (IREC) of Moi University (Approval No. FAN/ IREC 000554). Informed consent was sought and obtained from caregivers involved; all participants were assured of confidentiality.

RESULTS

Demographic information of the children and their caregivers: In this study, 230 HIV infected children aged between 3 and 14 years who had been on ARVs for at least three months before this study participated. They were aged between 3-14 years (mean age 8.5 years ±3.2 SD). Most of the children were in the age bracket of 9-11 years (30.9%). A large proportion were males, 134 (58.3%). The results showed that 54 (23.5%) of the children were orphaned by both parents, 85(37.8%) were orphaned by one parent, and 91 (39.6%) were non-orphaned. Majority of the children, 110 (47.8%) were in lower primary while 65 (28.3%) 52 (22.6%), were in pre-primary, and three (1.3%) had not started schooling.

Caregivers were aged between 16-90 years (mean age 34.6 years ± 10.4 SD) and a large proportion of them were female 178 (77.4%). Majority of them, 103 (44.8%) were between age bracket of 26-35 years. More than half of the caregivers were biological parents of the children, 137 (59.6%). Slightly more than half of caregivers were married, 125 (54.3%) were widowed while 35 (15.2%) were single. Majority of

the caregivers 184 (80%) resided in rural, as compared to 46 (20%) who lived in urban. The results indicated that about half 110 (47.8%) of the caregivers had primary education. About half the caregivers 104 (45.2%) were unemployed, and this affected more females 90 (50.6%) than males 14 (27.0%). This study indicated that majority of the caregivers 160 (69.2%) were farmers/business persons.

Factors Associated with ARVs drug Adherence
(i) Factors affecting time of giving ARV drugs to children:
Based on time of taking drugs by children, adherence levels was 56.2 %. The findings from binary logistic regression indicated that when caregiver was away from home (p=0.0010), it reduced the likelihood of adherence to time of taking drugs by 31%. When caregiver forgot to give drugs to the child (p=0.020), it decreased the probability of ARV drug adherence by 22%. Lack of disclosure (p=0.0080) and experience of side effects by the child (p=0.0120), decreased the likelihood of taking drugs on time by 29% and 28% respectively. The results indicated that lack of knowledge on treatment (p=0.0030) decreased the probability of adherence by 31%. Stigma (p=0.0470) reduced the likelihood of adherence to treatment time by 30% (Table 1).

Table 1
Adherence factors based on time of taking ARV drugs

Adherence factors	Co-efficient	Std. Err.	z	P>|z|	Marginal effects
Caregiver being away from home	-1.5654	0.4711	-3.3200	0.0010	-0.3050
Caregiver forgot to give drugs to child	-1.1363	0.4895	-2.3200	0.0200	-0.2200
Caregiver being too busy	0.1093	0.5661	0.1900	0.8470	0.0239
Lack of disclosure	-1.5021	0.5691	-2.6400	0.0080	-0.2879
Child experienced side effects	-1.5035	0.5966	-2.5200	0.0120	-0.2760
Child felt better	-0.1405	0.6421	-0.2200	0.8270	-0.0303
Early toxicity of drugs	0.7235	0.6460	1.1200	0.2630	0.1603
Depression experienced by child	1.0697	0.6925	1.5400	0.1220	0.2302
Child felt too ill	0.4270	0.6449	0.6600	0.5080	0.0916
Ran short of drugs	0.9298	0.6162	1.5100	0.1310	0.2038
Change in routine	-0.0370	0.5118	-0.0700	0.9420	-0.0080
Lack of belief in benefits of treatment	0.7561	0.5140	1.4700	0.1410	0.1644
Child forgot to take medicines	-0.9196	0.6271	-1.4700	0.1420	-0.1946
Lack of knowledge into treatment	-1.5393	0.5223	-2.9500	0.0030	-0.3053
Distance to facility was far	0.3372	0.5527	0.6100	0.5420	0.0734
Complex regimens (too many medicines)	-1.7406	0.8518	-2.0400	0.0410	-0.3103
Lack of insight into illness	0.8758	0.6341	1.3800	0.1670	0.1997
Severity of the disease	0.5534	0.7212	0.7700	0.4430	0.1235
Co-condition	-0.7228	0.5527	-1.3100	0.1910	-0.1464
Fear of child getting used to medicines	-0.2057	0.5984	-0.3400	0.7310	-0.0437
Food restrictions	0.5707	0.6277	0.9100	0.3630	0.1273
Child slept	-0.7821	0.4930	-1.5900	0.1130	-0.1609
Child refused to take medicines	0.0103	0.6050	0.0200	0.9860	0.0022
Child threw it up/vomited medicines	-0.3466	0.6213	-0.5600	0.5770	-0.0732
Clinic run out of medicines	-0.6955	0.7828	-0.8900	0.3740	-0.1393
Stigma	-1.6716	0.8408	-1.9900	0.0470	-0.3005
Ethnic background	-1.8271	1.4090	-1.3000	0.1950	-0.2677
Transport cost	-1.8745	1.2755	-1.4700	0.1420	-0.2908
Lack of social support	-2.5316	1.6188	-1.5600	0.1180	-0.3344
Constant	2.0924	0.4984	4.2000	0.0000	

ii). Adherence factors based on clinic appointments: The overall ARV drug adherence based on clinic appointments was 45.7%. The results from binary logistic regression analysis indicated that when a caregiver was away from home it decreased the probability of keeping clinic appointments by 32% (p=0.004). Lack of disclosure of HIV to the child, reduced the likelihood of keeping to treatment by 53% (p=0.0000). When the child experienced side effects of the drugs, it reduced the likelihood of keeping to clinic appointments by 40% (p= 0.0030). Stigma (p=0.0070) and transport cost (p=0.0240) decreased the probability of keeping to clinic appointments by 43% and 51% respectively (Table 2).

Table 2
Adherence factors based on clinic appointments

Adherence factors	Co-efficient	Std Err	Z	p|z|	Marginal effects
Caregiver being away from home	-1.3274	0.4656	-2.8500	0.0040	-0.319
Caregiver forgot to give drugs to child	-0.7353	0.4839	-1.5200	0.1290	-0.1812
Caregiver being too busy	0.8553	0.5527	1.5500	0.1220	0.20608
Lack of disclosure	-2.4020	0.6243	-3.8500	0.0000	-0.5255
Child experienced side effects	-1.7563	0.5851	-3.0000	0.0030	-0.4018
Child felt better	-0.3451	0.6167	-0.5600	0.5760	-0.086
Early toxicity of drugs	0.8142	0.6766	1.2000	0.2290	0.19977
Depression experienced by child	0.3933	0.6591	0.6000	0.5510	0.09795
Child felt too ill	0.4401	0.5988	0.7300	0.4620	0.10956
Ran short of drugs	1.1727	0.5996	1.9600	0.6500	0.28388
Change in routine	-0.0492	0.5086	-0.1000	0.9230	-0.0123
Lack of belief in benefits of treatment	0.7559	0.5465	1.3800	0.1670	0.18647
Child forgot to take medicines	-1.1499	0.6578	-1.7500	0.0800	-0.2798
Lack of knowledge into treatment	-0.3830	0.5077	-0.7500	0.4510	-0.0955
Distance to facility was far	0.0416	0.5332	0.0800	0.9380	0.0104
Complex regimens (too many medicines)	-0.3693	0.7687	-0.4800	0.6310	-0.092
Lack of insight into illness	0.9169	0.5925	1.5500	0.1220	0.22189
Severity of the disease	-0.6256	0.6635	-0.9400	0.3460	-0.1549
Co-condition	-0.0259	0.5514	-0.0500	0.9630	-0.0065
Fear of child getting used to medicines	0.5734	0.5561	1.0300	0.3030	0.14142
Food restrictions	-0.2514	0.6005	-0.4200	0.6750	-0.0628
Child slept	-0.8529	0.4950	-1.7200	0.0850	-0.2097
Child refused to take medicines	1.0337	0.6226	1.6600	0.0970	0.24699
Child threw it up/vomited medicines	0.6043	0.6136	0.9800	0.3250	0.14918
Clinic run out of medicines	-0.5683	0.6646	-0.8600	0.3920	-0.1408
Stigma	-1.9257	0.7119	-2.7100	0.0070	-0.4332
Ethnic background	-1.8645	1.4139	-1.3200	0.1870	-0.3884
Transport cost	-2.6796	1.1906	-2.2500	0.0240	-0.5082
Lack of social support	-2.6204	1.4544	-1.8000	0.0720	-0.4912
Constant	2.4396	0.5187	4.7000	0.0000	

DISCUSSION

The findings in this study established that factors that were associated with time of taking drugs by the children were: caregiver being away from home, caregiver forgot to give drugs to the child, lack of disclosure and experience of side effects of medicines by the child. Several studies have shown that caregiver being away from home, being too busy and forgetting to administer medications are interrelated and affect people who are in the early stages of disease (13, 14, 20). Lack of HIV disclosure and stigma to children influenced negatively adherence to time of taking ARV drugs in this study. This agreed with other studies which established that younger age, later stage disease, fear of HIV disclosure and stigma, adverse effects and forgetfulness was associated with poor adherence (10,11). The results did not agree with an Italian study of children over eighteen years which indicated that disclosure was associated with worse adherence (17). Studies in US and Ethiopia found similar results when controlling for potential covariates (19, 22). However, there was no effect seen for age or disclosure on adherence in US and in Ugandan studies (15, 23). Qualitative studies in Uganda and Belgium found that disclosure was generally associated with improved adherence (24). Based on the findings of this study, there is need for support disclosure of HIV status to children, family and other social institution, to increase HIV/AIDS community awareness to reduce stigma, and use of reminders to reduce forgetfulness of giving drugs to children by caregivers in order to improve adherence. In a situation where caregiver will be away from home, prior arrangement should be made for administering the drugs to the child to avoid non-adherence.

In this study experience of side effects was associated with adherence to time of taking ARV drugs. Other studies established that side effects have consistently been associated with decreased adherence and patients who experience more than two adverse reactions are less likely to continue with treatment (18). Patients may self adjust their regimens especially if they experience very bad side effects, toxicity or personal beliefs which in a way affect drug adherence (26). The study findings conformed with another study which noted that side effects from ARVs, compounded by factors related to caregivers and developmental challenges particularly in older children, contributed to non-adherence to ART in Jamaican children (12). Studies have established that complexities of ARVs, in addition to the problems of toxicities and side effects, can greatly influence an individual's willingness and ability to adhere to the therapy (27). Other studies have indicated that experience of side effects may lead to frustration and treatment fatigue, and also ultimately to poor adherence. There is need for caregiver and older children to be educated by health providers on the possible side effects of the medications.

Lack of knowledge on the treatment and insight into illness were associated with adherence in this study. Studies have shown that a patient's knowledge about disease and medication can influence adherence. Understanding the relationship between adherence and viral load and between viral load and disease progression is integral to good adherence behaviour. Difficulty in understanding instructions has also been reported to affect adherence. Other studies indicated that, 25% of the participants failed to understand how their medications were to be taken (28). Caregivers and older children need to continuously be given all the information regarding ARV drug adherence by health care providers to improve adherence.

Based on clinic appointments, factors that were associated with adherence were: caregiver being away from home, lack of disclosure, experience of side effects by a child and stigma. These were among the factors which affected adherence to time of taking drugs. It has been reported that being away from home, being too busy and forgetting are interrelated and affect people who are in the early stages of the disease (21, 8). Forgetfulness and being too busy have been cited as the most common reasons for poor adherence to medications. Transport cost also affected adherence to clinic appointments. Other studies established that transport costs were among other barriers which influenced adherence among the children on ARV treatment (29). Studies have shown that denial and fear of HIV status, misinformation about HIV, low availability, accessibility and acceptance of therapy are some of the issues affecting adherence in HIV infected adolescents (16). Despite provision of free ARV treatment, lack of transport influenced adherence to clinic appointments. Since majority of the caregivers resided in rural areas, transport cost affected adherence to clinic appointments. There is need to put in place mechanisms that will decentralise HIV/AIDS services closure to the patients in the community.

In conclusion, the factors that were associated with adherence to ARVs by children were; caregiver being away from home, caregiver forgetting to give drugs to child, lack of disclosure, child experiencing side effects of the ARV drugs, lack of knowledge into treatment, stigma and transport costs. It was recommended that there is need to design specific interventions strategies addressing the identified factors associated with non-adherence to ARVs in HIV infected children under care of caregivers. The use of reminders for caregivers to give ARVs on schedule and administration of simpler ARV drug regimens with less side effects should be considered together with other measures to enhance adherence in children.

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