

**FACTORS INFLUENCING ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG
HIV INFECTED CHILDREN ATTENDING THE DAY CARE HOSPITAL AT THE
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ABSTRACT

Paediatric adherence to antiretroviral therapy (ART) is important in achieving efficiency of treatment and preventing failure to therapy. The aim of this study was to determine the rate of adherence to ART and identify factors influencing adherence to paediatric ART at the Day Hospital of the Bamenda Regional Hospital. We conducted a cross-sectional study with 213 children (≤ 14 years old) who were on antiretroviral therapy for at least six months. Adherence was assessed retrospectively, through self-administered questionnaires to the patients or their caregivers. An adherence rate of $\geq 95\%$ was considered accepted as optimal adherence. Data was analyzed using SPSS version 20.0 (SPSS Inc Chicago USA) statistical packages. Overall, the adherence rate for the 213 participants was 26.8%. Significantly low levels of adherence were observed among caregivers who either had no formal education, were grandparents and had formal employment ($P < 0.05$). The major patients' factors associated to non-adherence was refusal to take medicine while forgetfulness by caregivers accounted for the majority caregivers' factor. The highest number of caregivers who forgot to administer medicine were those with primary education, grandparents and the self-employed. Poor attitude of health care provider and long waiting time at the clinic were the major reasons for non-adherence. Paediatric adherence to ARV at this Day Care Hospital is low. The patient, caregiver, health-care-provider, and the health facility all contribute to this frightening percentage of non-adherence.

KEYWORDS: adherence, antiretroviral therapy, paediatrics, factors, HIV, Cameroon.**INTRODUCTION**

HIV/AIDS remains one of the major leading cause of death among adolescents in Africa with an average of 328 deaths per day recorded among children in 2016.^[1] The majority of children living with HIV acquired the infection through the 'vertical transmission' or parent-to-child-transmission' mode either during pregnancy, childbirth or breastfeeding. One of the most devastating impacts of HIV on children is the loss of parents or older relatives. Of the estimated 13.4 million children and adolescents worldwide, who are orphans due to AIDS as of 2015, more than 80% of them live in sub-Saharan Africa.^[2]

Generally, antiretroviral therapy (ART) has played an important role in improving the quality of life of HIV/AIDS patients, and in reducing the rate of disease progression and death.^[3] Without ART, one third of infants with HIV do not reach their first birthday while

50% do not reach two years of age.^[4] Regrettably, in paediatric formulations, there is limited range of age-appropriate antiretroviral drugs which are available thus making treatment more challenging. Antiretroviral medicine suppresses the virus replication thus reducing the destruction of CD₄⁺ cells and consequently slow the progression of the disease.^[5] Unfortunately, access to the medicine is a major limitation in the affected areas. UNAIDS reported that out of the estimated 1.8 million children living with HIV in 2016, only 43% had access to antiretrovirals.^[6] Even though there has been an improvement in treatment coverage since 2010, when just 21% of children living with HIV were on ART, the current coverage indicates that a lot still need to be done.

Antiretroviral therapy adherence is a primary determinant of the effectiveness of this treatment and is also considered a major predictor of survival among patients living with HIV/AIDS.^[7] More than 95%

adherence to ART is required to prevent the emergence of resistant HIV strains, obtain long-term HIV suppression, reduce destruction of CD₄⁺ cells, increase survival, and improve quality of life.^[8] On the other hand, poor adherence to antiretrovirals can create a dangerous public health problem and limit the effectiveness of available HIV treatments.

Although HIV treatments for children works, the effectiveness of this therapy depends on high levels of adherence. The challenges and complexities of present treatment which includes antiretroviral regimen contribute to non-adherence. Patient and family/caregiver related factors are among the three groups of factors that have been shown to influence adherence in children. The fact that children are dependent on adult or caregivers to follow the treatment, present additional complications to adherence issues.^[9] Adherence in children requires a compliant child and a committed primary caregiver. Medication related challenges includes the palatability of drugs, the volume of medicines recommended for children and storage conditions which might be an issue in some countries.^[6] Some antiretroviral medications have been associated with significant short- and long-term adverse effects such as nausea, rashes, hypersensitivity reactions while others still need to be taken with food, so care-givers may have to perform the task of providing a meal and administering drugs simultaneously.

Caregivers related challenges include amongst others an unwillingness to publicly disclose the child's HIV status. Moodley and others^[10] reported an HIV disclosure rate of 26% among children older than 6 years in South Africa. Reasons for non-disclosure includes the social stigma that surrounds the disease, the psychological impact on the child and social rejection/discrimination. Another reason is the existence of an antagonism to the person delivering the therapy. The regimens also include medicines that may have complex dosing schedules and may cause food interruptions and adverse effects resulting in poor tolerability.^[11] If the caregiver is infected then he/she is struggling with his/her own illness, psychosocial factors, medication regimes and most often financial burden due to expenses incurred on his/her own therapy and associated cost of medical treatment.^[9,12] These factors along with his /her own knowledge about ART can interfere with caregiver's ability to provide proper care to the child, thereby affecting the necessary adherence to ART over time.^[13] The aim of this cross-sectional study was to determine the adherence rate to antiretroviral medicine and identify factors influencing adherence among HIV-infected children at the Day Hospital of the Bamenda Regional Hospital.

MATERIALS AND METHODS

Study setting, design and population

The study was carried out in the Day Hospital of the Bamenda Regional Hospital. This section of the hospital

takes care of HIV positive clients including refill of antiretroviral drugs and counselling. This was a cross-sectional study that evaluated the rate of adherence to ARV and factors influencing adherence in this health facility among 213 children who have been on treatment for at least six months. The study was conducted in April and May 2018. Patients who were ≤ 14 years and who attended routine clinic visits during the recruitment period and gave informed consent were considered for inclusion in the study.

Evaluation of adherence and associated factors

Adherence, extent to which the prescribed medication was taken and according to medical recommendations as well as factors responsible for missed doses were assessed retrospectively via questionnaires administered to the patients or their caregivers. Procedures for completing the questionnaire were individually explained to each participant in a quiet place respecting the respondent's confidentiality. The structured questionnaire was pre-tested on 25 caregivers not involved in the study nor in the study site. The questionnaire was divided into four sections comprising socio-demographic characteristics (age, gender and caregiver's level of education, source of income, relationship with the child, and the parental status of the child); patient and caregiver factors associated with adherence (variables included side effect of drugs, pill burden, caregiver's availability, forgetfulness, fear of disclosure of status and shortage of drugs); and health personnel/health facility-linked factors (variables included rudeness of staff, appointment dates, distance to the clinic, unclear instructions on how medication should be taken, long waiting time, no respect of personality and privacy). The dependent variable in this study was "adherence/non-adherence" while the independent variables consisted of characteristics that theoretically could influence adherence/non-adherence. These were the sociodemographic characteristics, patient and caregiver factors and health personnel and health facility associated factors. An adherence rate of equal to or greater than 95% was considered accepted as optimal adherence.^[5]

Statistical analysis

The generated data was analyzed using SPSS version 20.0 (SPSS Inc Chicago USA) statistical packages. Proportions were compared using either the chi-square test or Fisher's exact test. Differences between adherence, non-adherence groups and independent variables were considered to be significant if $P \leq 0.05$.

Ethical Statement

Ethical clearance for the study was obtained from the Institutional Review Board of the University of Bamenda, Cameroon (2018/0053/UBa/IRB). Informed consent was got from the participants' caregiver before enrolling them in the study. All interviews took place in private and the information obtained was handled with

utmost confidentiality. Serial numbers and codes were used to ensure non-disclosure of the of the client.

RESULTS

Sociodemographic characteristics of the study population: Out of the 213 children that were recruited in this study, 119 (55.9%) were females and the highest number of participants were in the age group 5-10 years old (41.3%). Most of the caregivers (48.4%) had attained only primary level of education and 96 (44.6%) of them were the biological mothers of the children. A greater proportion (48.8%) of the caregivers were unemployed and 77 (36.2%) indicated that both parents of the infected children were deceased. The children who had been on ARV for 3-5 years constituted the greater majority (47.4%).

Rate of adherence to antiretroviral drug (ARV):

Overall, the adherence rate for the 213 participants was

26.8% (57/213). As detailed in Table 1, females, and those between 10 to 14 years recorded the highest rate of adherence. There was a significant difference in adherence among parents of children who had attained secondary level of education ($p=0.004$). The child adhered more to treatment when the caregiver was the biological father ($p=0.001$). Children whose caregivers were unemployed equally adhered more ($p=0.044$) while those with formal employment recorded the least adherence of their children to treatment (Table 1).

Patients' and caregivers' factors influencing adherence:

Of the patients' related factors responsible for non-adherence, refusal to take medicine recorded the highest (46%). As shown in figure 1, pill burden accounted for the least of the factors responsible for non-adherence.

Table 1: Rate of adherence to ARV by sociodemographic characteristics of patient and their caregivers (N=213).

Variables		Adherence N=57	Non-adherence N=156	Level of significance
Sex	Male	20 (35.1)	74 (47.4)	$\chi^2=2.582$ $P=0.108$
	Female	37 (64.9)	82 (52.6)	
Age group	Less than one year	3 (21.4)	11 (78.6)	$\chi^2=0.405$ $P=0.939$
	Between 1 and 5 years	8 (24.2)	25 (75.8)	
	Between 5 and 10 years	24 (27.3)	64 (72.7)	
	Between 10 and 14 years	22 (28.2)	56 (71.8)	
Educational level of caregivers	No formal education	3 (5.3)	19 (12.2)	$\chi^2=11.10$ $P=0.004$
	Primary	20 (35.1)	83 (53.2)	
	Secondary	34 (59.6)	54 (34.6)	
Relationship of caregiver to child	Biological mother	27 (47.4)	68 (43.6)	$\chi^2=22.77$ $P=0.001$
	Biological father	12 (21.1)	12 (7.7)	
	Sibling	6 (10.5)	29 (18.6)	
	Grand parent	10 (17.5)	13 (8.3)	
	Self-care	2 (3.5)	34 (21.8)	
Caregiver's source of income	Formal employment	10 (17.5)	10 (6.4)	$\chi^2=6.229$ $P=0.044$
	Self-employed	14 (24.6)	48 (30.8)	
	Unemployed	33 (57.9)	98 (62.8)	

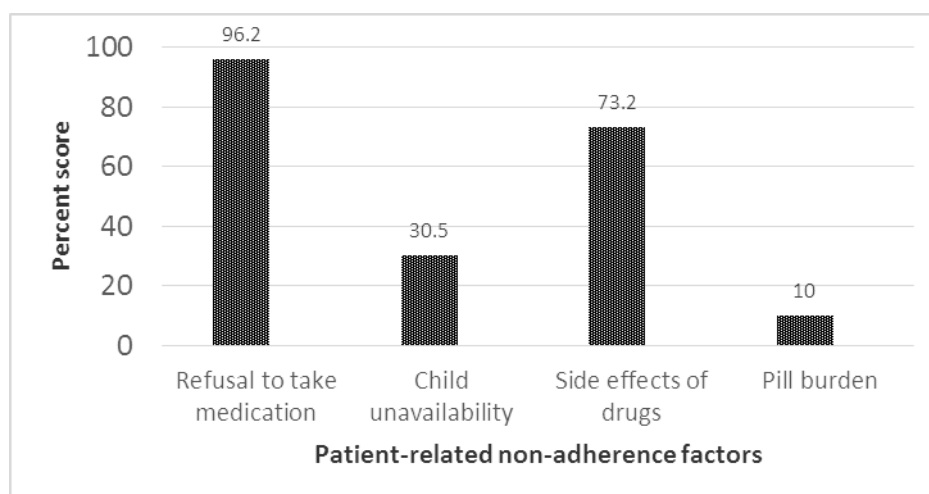


Figure 1: Patients' related adherence difficulties.

Side effects of the drug was reported in 156 (73.2%) children who were on either first- or second-line treatment. The highest percentage of children (57.7%) who suffered side effects were those on second line treatment. Patients placed on Douvir/Efavirenz, a first

line drug and Tenolam/Kalatra, a second line drug recorded the highest number of cases with side effect (Table 2). The major side effects reported by the caregivers were: dizziness, fever, reddish eyes, sweating and vomiting.

Table 2: Distribution of side effects according to drug category.

Drugs	Frequency (%) n=213	N ^o of patients with side effect; n=156	N ^o of patients without side effect; n=57
First line	89(41.8)	66(42.3%)	23(40.4%)
Douvir/N	11 (5.2)	7(10.6%)	4(17.4)
Douvir/Efavirenz	39(18.3)	34 (51.5%)	4(17.4)
Tenolam/N	39(18.3)	25(37.9%)	14(60.9)
Second line	124(58.2)	90(57.7%)	34(59.6%)
Tenolam/Kalatra	41(19.2)	35(38.9%)	6(17.6)
Douvir/Atazanavir	42(19.7)	23(25.6%)	19(55.9)
Abacalam/Kaletra	41(19.2)	32(35.6%)	9(26.5)

Eight major factors were identified as influencing adherence to ARV in these children. Of these, forgetfulness by caregivers accounted for the majority (42.7%) while the least (2.3%) was improvement in the child's health (Figure 2). We observed that the category

with the highest percentage of caregivers who forgot to administer the child's medicine were either those who had attained only primary level of education (43.7%), were grandparents to the children (52.4%), or those who were self-employed (45.2%).

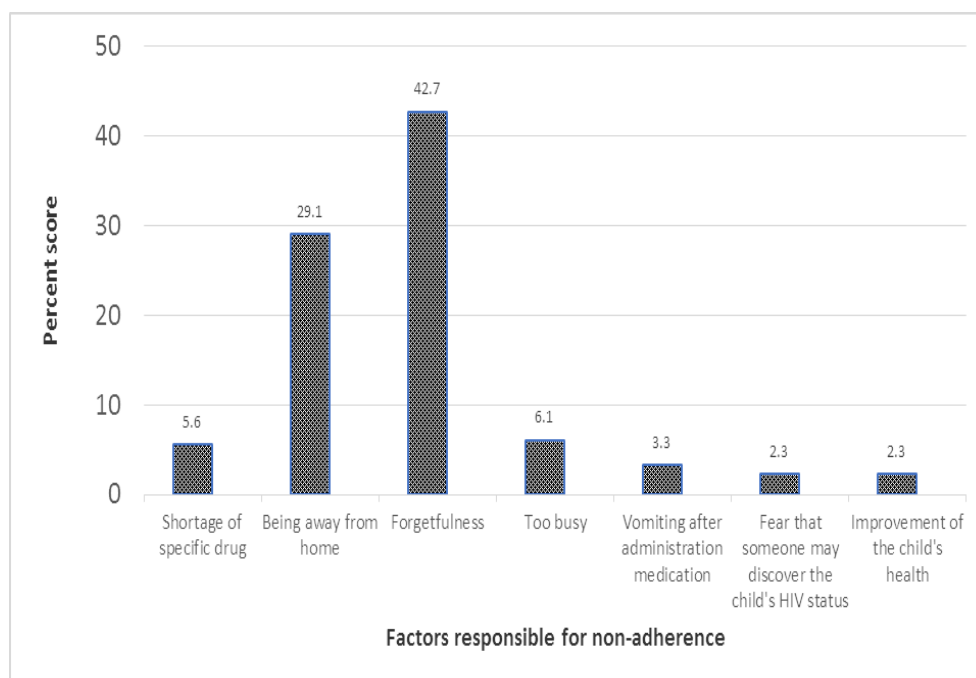


Figure 2: Caregivers variables contributing to non-adherence.

Health personnel and health facility factors influencing adherence to ARV by patients: Attitude and practices of health care personnel toward the patients during drug refill were responsible for more than 50% of non-adherence. Of these, poor attitude of staff in the clinic toward the patient registered the highest (77.5%) followed by non-effective reminder strategies for the caregivers to administer the child's drugs (63.4%). Slightly above half of the respondents (54.9%) indicated that the staff do not give clear instructions on how medication should be taken while 53.1% stated that there was no respect of personality, privacy, and

confidentiality. Also, 52.6% of the respondents reported that the staff do not pay keen attention to the patients/caregivers during hospital visits.

With regards to the health facility, the location of the establishment was the major factor. Respondents indicated that long waiting time at the Treatment Centre was the major reason for non-adherence (94.8%) followed by the distance to the Centre which is more demanding financially (Figure 3).

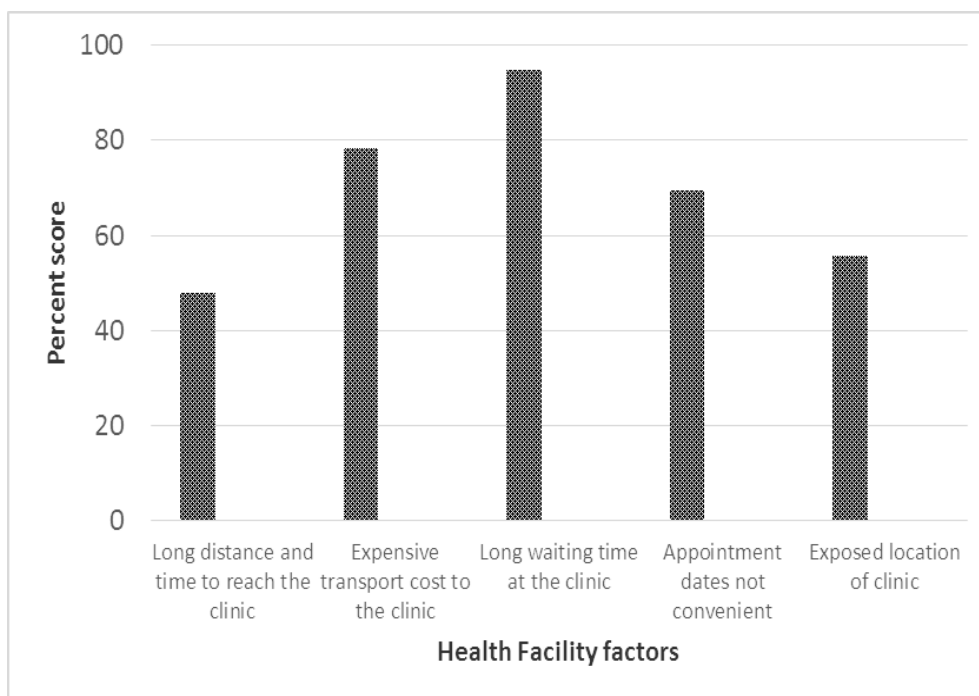


Figure 3: Health associated factors influencing adherence.

DISCUSSION

The current study revealed that the adherence rate to ARV among 213 children attending the Treatment Centre of the Bamenda Regional Hospital was 26.8%. Children of caregivers who had attained secondary level of education and those that were the biological fathers of the children adhered more to treatment. The major factors identified to be responsible for non-adherence were refusal to take medication by the child, forgetfulness to administer medicine by the caregivers, the poor attitude of the hospital staff toward the caregiver and long waiting time at the hospital during drug refill appointments.

The low adherence rate of 26.8% recorded in this study is slightly higher (24.6%) than what was observed in a similar study conducted in Kilimanjaro, Tanzania^[14], and Yaoundé, Cameroon^[15] but lower in most studies conducted in Africa and beyond.^[5,16-18] Unlike many studies where the participants were either adolescents or adults, this study had more of children with their respective caregivers as respondents. In this study, more than half of the caregivers had attained only primary level of education and were also unemployed. These characteristics could influence the rate of adherence as knowledge and other preoccupations could possibly serve as contributing factors. Other studies, however, did not show any association between level of education and adherence.^[19]

The major patients' factors responsible for non-adherence was refusal of the child to take medicine (96.2%) followed by side effects of the drug (73.2%). This observation corroborates with Osterberg and Blaschke^[11], who reported that refusal to take medication by the child is a major reason for non-adherence. Refusal

of young children to take medication has plethora of reasons amongst which are: an inability to swallow tablets, side effects, a dislike to the taste; feeling unwell and hence refusing to cooperate. The person administering the drug may display poor attitude that does not encourage the child to take the medicine. Furthermore, the medicines may have complex dosing schedules which may cause food interruptions and adverse effects resulting in poor tolerability. This could justify our observation as 135 of the children under study were aged ≤ 10 years.

On the caregivers' site, forgetfulness and being away from home were responsible for respectively, 42.7% and 29.1% of non-adherence cases. This observation strongly supports the findings of Reddington *et al.*^[9] and other studies conducted in Myanmar, sub-Saharan Africa, and Indonesia^[17,20-21] on the factors influencing adherence. We observed that the highest number of people who forgot to administer medicine were those with primary education, grandparents and the self-employed. It is likely that a child can miss taking medicine because the caregiver forgets to do so especially in the absence of a reminder strategy in place. Having grandparents in this group is not unusual considering that there is a drop in memory with age owing to the deterioration of the hippocampus in the brain. Due to other responsibilities with making ends meet, the possibility of the self-employed forgetting the time of administering medicine is high. Our observation of those having only primary education also found in this category could be related to the influence of knowledge on the importance of prompt dosing. Unpleasant side effects like vomiting, sweating, and dizziness can cause the caregiver to stop giving the medication, hence leading to non-adherence.

Most of the children above 5 years were not aware of their status, and of these, 77.5% of them missed their drugs when the caregivers are away from home. Feeling unwell and ignorance could contribute to this. It is important for the child to know his/her status and the reason for medication. Educating the child on the benefits of proper and prompt treatment may improve adherence. In addition, disclosing the child's status to some reliable neighbours can lead to proper follow-up of the child in the absence of the caregiver thus improving adherence. Aye and others in Myanmar^[17] reported an improvement in adherence when the status was disclosed to others.

For children who adhered most to treatment, their caregivers had either attained secondary education, were their biological fathers or had formal employment. This support the impact of knowledge and "emotional" attachment on dosing adherence.

Low level of adherence was associated to the poor attitude of the health care providers. Rudeness of the health care providers was reported by 77.5% of the respondents ranking it as the major factor accounting for non-adherence. This poor attitude towards either the caregiver or the patient can be traumatizing, most especially, as these patients have extra challenges such as stigma and illness to cope with. Our results are consistent with those of Roberson *et al.*^[22] and Stone *et al.*^[23] Some relationships with health care providers could be barriers or facilitators of adherence. A good patient-health care provider relationship can serve as a facilitator for adherence even to unpleasant complex drugs.^[23] In most health care in the developing world, the number of workers is few with the result of high patient to staff ratio. Unfortunately, in such resource limited areas, there is no commensurate increase in the pay package. These "hard-pressed" and often disgruntled workers can lose their temper. Frustration of health-care providers is also associated with lack of patient adherence to treatment, miscommunication, and missed appointments. Not of the patients' making, the complexity of treatment regimens, and the side effects of the medication can also discourage the health care provider and affect the relationship with the client.^[24]

Long waiting time (98.8%), distance to the health facility (78.4%), inconvenient appointment dates (69.5%) and the exposed nature of the health facility (55.9%) were indicated as barriers to adherence. These barriers are consistent with reports by Weaver in Indonesia.^[21] When the patients stay for long at the clinic, it leads to demotivation and this might affect their adherence and healing process. Increasing the staff manpower as well as motivational tools to the staff can reduce waiting time and hence increase adherence. Long distance to the health care facility is equally financially demanding. Boyd-Franklin *et al.*,^[25] and Mafune *et al.*^[26] indicated that the lack of finances can impair the families' ability to manage the children's illness, including the proper

administration of medications. Decentralization of clinic centres is necessary as it will reduce money spent on transport and increase the welfare of the client. Inconvenient appointment dates cause the clients to miss appointments while an exposed health setting can scare away patients from the clinic for fear of being exposed.

The strength of this study is the novel data on paediatric adherence rate to ART in Bamenda, Cameroon. It has also identified new key factors linked to non-adherence among children. One limitation recognized in this study was the complete reliance on self-reporting on adherence by the caregivers. Other tools which could be more objective such as electronic pill caps were not used. That notwithstanding, our current method has been reported in other studies. The respondents were counselled, encouraged, and provided an environment that support honest responses.

CONCLUSIONS

Despite counselling on the importance to drug adherence before initiation to treatment and during drug refill, paediatric adherence to ARV is still sub-optimal. Refusal to take medicine by the child, forgetfulness to administer medicine by the caregiver, poor attitude of healthcare provider and long waiting time at the health centre are the major barriers responsible for non-adherence. There is an urgent need to improve paediatric adherence else the beneficial effect of ART will be forfeited in this health area.

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