

**CARE-GIVER FACTORS ASSOCIATED WITH ADHERENCE TO  
ANTIRETROVIRAL THERAPY IN HIV INFECTED CHILDREN: A CASE  
OF THIKA DISTRICT HOSPITAL IN KENYA**

**By**

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**DECLARATION**

This Thesis is my original work and has not been presented for a degree in any other university.

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## **DEDICATION**

This work is dedicated to the many children living with HIV/AIDS and their health and primary caregivers'; may this work provide solutions to the challenging responsibility of ensuring optimal adherence to pediatric ART.

## **ACKNOWLEDGEMENT**

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**ACRONYMS AND ABBREVIATIONS**

<b>AIDS</b>	Acquired Immune Deficiency Syndrome
<b>ART</b>	Antiretroviral Therapy
<b>ARV</b>	Antiretroviral
<b>HIV</b>	Human Immune Deficiency Virus
<b>24RI</b>	24 Hour Recall Interview
<b>HAART</b>	Highly Active Antiretroviral Treatment/Therapy
<b>UNAID</b>	United Nations Aid.
<b>WHO</b>	World Health Organization
<b>UNICEF</b>	United Nations Children's Fund

## DEFINITION OF TERMS

- Adherence** Is described as the engagement and accurate participation of an informed patient in a plan of care. The concept of ‘adherence’ has a broader meaning than compliance. It encompasses the extent to which a patient follows instructions and implies understanding, entering into and continuing in a programme or care, plan, as well as keeping appointments and tests as scheduled (Rabkin *et al.*, 2003).  
Adherence to HAART is most often defined as the extent to which the prescribed number of pills is taken in the prescribed number of daily doses. To be most effective, however, HAART regimens often require that patients are adherent to other recommendations, such as following strict dosing schedules and following food and fluid intakes, requirements and restrictions.
- Non-Adherence** Means not following the prescribed treatment plan and includes missed or delayed doses or failing to follow guidelines like, taking too little or too much medication and taking it at incorrect times. Non adherence can vary from missing one dose of a medication, to missing a single dose of all three or four drug combinations, to missing doses or all doses a day or week. Not observing instructions regarding dietary or fluid intake or not taking medications at prescribed time intervals also constitutes non –adherence.
- Primary Caregiver** A person who has consistently assumed responsibility for the housing, health, or safety of the child (individuals who administered at least 50% of the child’s medication daily and bringing the child for clinic appointments).

**ABSTRACT**

Survival of children with AIDS has increased considerably with the use of effective antiretroviral drugs, but the benefits of this therapy are limited by the difficulty of adherence to the treatment. This cross-sectional study was aimed at estimating the prevalence of adherence to antiretrovirals and identifying the associated caregiver factors affecting adherence among children resident in Thika town. Two hundred child caregivers were interviewed. The 24 Hour Recall Interview technique utilized to evaluate adherence prevalence allowed the detection of conscious loss of dose/s. Adherence was defined when the child had taken 100% of the prescribed medication during 24 hour period prior to the interview. Non-adherence was defined when the child missed even one dose of a medication during the 24 hour period prior to the interview. A general prevalence of adherence/non-adherence was established. The data was processed using SPSS 12.0 and Epi info 6.0 statistical packages. The significance of the findings was determined by Chi-square test and Logistic regression was used to remove the effect of confounding variables. The rate of adherence at Thika District Hospital was found to be 42%, meaning that pediatric adherence to ART in this setting is a challenge. Primary caregivers' ability to follow the child's ART based on the rigorous schedules  $\chi^2=35.31:1df$ :  $p<0.05$  [0.001] and primary caregivers drug related problems/difficulties  $\chi^2=60.07:1df$ :  $p$  [0.001] were associated with adherence to ART in bivariate analysis. Those able to follow the child's ART showed better adherence. The most reported drug related difficulties/problems were administration interfering with lifestyle and drug side effects. Adherence was independently associated with primary caregivers relationship with the child  $p<0.05$  [0.018]. The fact that the primary caregiver was a parent of the infected child adversely affected adherence. The Primary caregivers level of education was also independently associated with adherence  $p<0.05$  [0.005]. Adherence rate was seen to increase with increasing primary caregiver level of education. There is thus need for assessments of the caregivers' level of education, relationship to the child, their ability to administer treatment, need for continuous assessment of caregivers' knowledge on ART, continuous assessment of adherence and scheduling treatment to meet the caregivers' lifestyle in an effort to ensure improved adherence to ART in Thika District.

## CHAPTER ONE: INTRODUCTION

### I.1 Background

Acquired Immunodeficiency Syndrome(AIDS), one of the most destructive epidemics the world has ever witnessed; claimed 3.1 million [2.8 – 3.6 million] lives in 2005 of which more than half a million [ 570,000] were children. By July 2007, an estimated 2.1 million [1.99-2.4 million] children were living with HIV worldwide, with 290,000 (270,000-320,000) succumbing to the disease (UNAIDS, 2007). Therapeutic strategies have expanded greatly from historical treatment with a single antiretroviral drug to combination therapy that includes at least three different drugs from up to three different classes; HAART. The three classes that make up HAART regimes are nucleoside analog reverse transcriptase (NRTI) inhibitors, non-nucleoside analog RT inhibitors (NNRTI) and protease inhibitors (PI). There are a number of ARVs approved for treatment in children, both first and second line treatment. (UNAIDS, 2007). These come in various formulations (Appendix 4).

Use of antiretroviral drugs in combined therapy has decisively altered the course of the HIV/AIDS infection epidemic. Antiretrovirals control the HIV infection, interfering with viral replication and thus drastically reducing the morbidity/mortality of AIDS. (Yamashita *et al.*, 2001). For children with HIV infection, recent advances in the use of antiretroviral therapies have significantly improved life expectancy (Abrams *et al.*, 2001; De Martino *et al.*, 2000; Gortmaker *et al.*, 2001). Without ART, one third of infants with HIV do not reach their first birthday; 50% do not reach two years of age ([www.hivimplementers.org/pdf/poster](http://www.hivimplementers.org/pdf/poster)). For these reasons HAART is

recommended for all adults, children and adolescents infected with HIV. Widespread acceptability and use of HAART has thus turned HIV infection into a chronic manageable disease (Naima *et al.*, 2004).

Many factors can affect the ability of HAART to suppress viral replication; including low potency of one of the drugs in the combination; viral resistance; inadequate drug exposure, and inadequate adherence to therapy. The major factor determining the success of HAART is sustained and optimum adherence to therapy (Starace *et al.*, 2006) as poor adherence increases the risk of virologic failure and viral resistance (Nischal *et al.*, 2005). Strict detailed adherence to physician prescribed HAART regimen has been shown to be clinically beneficial. Adherent individuals have been shown to have reduced viral load and increased CD4 counts, live longer and have better quality adjusted life years (Richter *et al.*, 1998).

However, as with other chronic pediatric diseases (Divertie, 2002; Fink, 2001), adherence to the complex antiretroviral regimens has been identified as a major barrier to realizing the full potential of the treatments. The effectiveness of antiretroviral therapy depends on high levels of adherence and the complexities of present antiretroviral regimes contribute to non-adherence (Ceccato *et al.*, 2004). 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 caregivers to follow the treatment, present additional complications (Reddington *et al.*, 2000). Adherence in children requires a compliant child and a committed primary caregiver. However, a young child may refuse to take the medication for a variety of reasons such as an inability to swallow tablets, an

aversion to the taste; feeling unwell and hence refusing to cooperate. There may also be an antagonism to the person delivering the therapy. The regimes also include medicines that may have complex dosing schedules and may cause food interruptions and adverse effects resulting in poor tolerability (Lars Osterberg *et al.*, 2005).

Family has also been shown to play a crucial role in any kind of treatment in children. Major issues related to family or caregiver that influence adherence include; presence of HIV infection in another member, fear of disclosure of HIV-positivity of the family, family disruptions and belonging to vulnerable groups. 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.(Descamps *et al.*,2000;Mellins *et al.*,2004;Reddington *et al.*,2000). 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 HAART over time (Chesney, 2000).

Sustaining adherence represents a significant challenge for children getting treatment, their caregivers as well as the healthcare providers. In order to facilitate adherence to HAART and increase treatment outcomes in HIV infected children, it is necessary to know possible and relevant issues in pediatric patients that influence adherence and determine possible interventions to improve adherence in children. There is need therefore to conduct studies to establish adherence rates and identify the family/caregiver factors affecting/associated with adherence. This will help increase the understanding and enhancement of HIV treatment adherence in pediatric patients.

## **1.2 Problem Statement**

It is now well established that optimum adherence for HAART is critical to successful outcomes of patients receiving therapy. At least 95% adherence to HAART is optimum and studies have shown that less than 95% adherence is associated with virologic failure rate of 75%. Among the factors that can influence treatment success or failure, research has identified high adherence to ART regimen as the most important predictor of viral suppression, improved CD4+ T Cell count, delayed progression to AIDS and patient survival. However, ensuring a high level of adherence is very difficult in cases of children on ART. Patient and family/caregiver related issues makes adherence to HAART in children very challenging. There is need therefore to identify the caregiver factors associated with adherence as this will help improve adherence in children thus increasing the likelihood of suppressing the virus, postponing the disease progression, decreasing morbidity associated with HIV and improving the quality of life in children infected with HIV. Improving adherence also helps reduce resistance thus reduces exposure to resistant strains of HIV virus and the need for expensive second line treatment.

## **1.3 Study justification**

In Kenya, the number of children between 1-14 years infected with HIV by December 2007 was between 140,000 and 170,000; with 15090 on ART treatment. There are 345 sites providing ART to children (WHO, UNAIDS, UNICEF, 2008).The Kenyan government and Non-Governmental organizations are scaling up HIV and AIDS treatment in children. Despite improvements in antiretroviral therapy and free access to these medications in Kenya, many patients are not benefited by the treatment. The ability of HIV-infected children to adhere to ART is essential to delay

resistance and ensure lifelong effective treatment. However, adherence is deemed as the most significant challenge to children receiving ARVs. If the child does not manage to adhere to treatment, the quality of life deteriorates over time, there is increased child mortality as a result of HIV or the child can and is affected by drug resistance and may need to begin second line drug regimes. The drugs required for this are generally too expensive to be provided in resource poor countries, Kenya being one such country.

As there are a few studies of child adherence, and factors relating to their caretakers interference with adherence in Kenya, the idea is, with the realization of the present study at Thika District Hospital, to collaborate with teams of health professionals that do follow-up AIDS infected children from birth-12 years of age, offering them information about adherence rates and risk factors. This will help to strengthen and sustain approaches for maintaining high treatment adherence among HIV seropositive children in the country using available and affordable first line drugs, improve their quality of life and reduce morbidity resulting from non-adherence to ART.

#### **1.4 Null hypothesis**

There are primary caregiver factors associated with adherence to ART in pediatric HIV infected children at Thika District Hospital.

#### **1.5 Objectives**

##### **1.5.1 Broad Objective**

- To describe the care-giver factors associated with adherence to ART among children at Thika District Hospital.

### **1.5.2 Specific Objectives**

- To determine the rate of adherence to ARV therapy among HIV infected children at Thika District Hospital.
- To determine the caregiver factors associated with pediatric adherence to ART at Thika District Hospital.
- To identify the drug related adherence difficulties among caregivers at Thika District Hospital.

### **1.5.3 Research Questions**

- What proportion of children with HIV/AIDS adheres to ART at Thika District Hospital?
- What primary caregiver factors are associated with adherence to ART among children with HIV at Thika District Hospital?
- What are the drug related adherence difficulties among primary caregivers of children at Thika District Hospital?

### **1.5.4 The Conceptual Framework**

This study focuses on the association between respondent's (primary caregiver) socio-demographic characteristics (gender, age, marital status, relationship to the child) socio-economic characteristics (level of education, financial status) and knowledge/attitudes towards ART as the independent variables, and adherence/non-adherence as the dependent variable (Fig 1.1).

**Figure 1.1 Conceptualized relationships among variables****Independent Variables****Socio-demographic Characteristics**

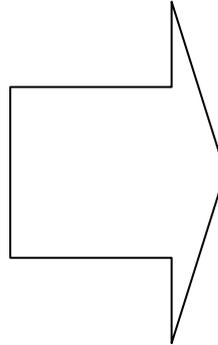
- Gender of primary caregiver
- Age of primary caregiver
- Marital Status of primary caregiver
- Primary caregiver relationship to the child

**Social-economic characteristics**

- Education level of the primary caregiver.
- Financial status of primary caregiver

**Knowledge and attitude towards ART.**

- Caregivers perceived problems administering ART

**Dependent Variables****Adherence / Non-Adherence**

## CHAPTER TWO: LITERATURE REVIEW

Large numbers of children have chronic illnesses requiring treatment regimens that are complex and need to be managed over the course of a lifetime. Such illnesses include asthma, diabetes, cystic fibrosis, rheumatic diseases, and, more recently, Human Immunodeficiency Virus (HIV). Recent studies in adults indicate that at least 95% treatment adherence is crucial for HIV/AIDS management (Carpenter *et al.*, 2000; Patterson *et al.*, 2000), and that even brief episodes of missed medication doses can permanently undermine HIV treatment, leading to reduced efficacy of and increased resistance to medications (Bangsberg *et al.*, 2000).

### 2.1 Pediatric Adherence Rates

A study in Brazil evaluated the effectiveness of treatment at different degrees of adherence in adults and concluded that plasmatic viremia was undetectable in 81% of cases where use level was 95% or more of prescribed dosages, 64% in those individuals that took 90-94% of prescribed dosages, 50% in cases that used 80-90% of the doses prescribed, 25% in cases that used 70-80% of the prescribed doses and 6% in cases the used less that 70% of the doses prescribed (Patterson *et al.*, 2000).

The few studies of adherence to antiretroviral regimens in children suggest that only 25% to 50% of HIV-infected children are adherent to all doses of their regime (Falkenberg, 1999; Reddington *et al.*, 2000).

Mellins *et al.*,(2004) used a battery of psychological assessments and self-reports adherence data in their study of caregivers and 48 HIV infected children aged 7 years

or more. Missed doses in the past month were reported by 40% caregivers and 56% of children. In a study to assess pediatric adherence to ART in Toto, West Africa, only 42% caregivers declared perfect adherence (Julie *et al.*, 2008).

## **2.2 Challenges to Adherence in Hiv Infected Children**

The challenges to adherence in HIV-infected children are numerous (Albano *et al.*, 1999; Fish *et al.*, 2001).

### **2.2.1 Medication Related Challenges**

Many children are unaware of their disease and are dependent on adults for their care (Mellins *et al.*, 2001).

Antiretroviral medications generally require frequent dosing and are supplied in formulations that may be difficult for children to tolerate (large pills, bitter-tasting liquids, and gritty powders).

Antiretroviral medications have been associated with significant short- and long-term adverse effects (nausea, rashes, hypersensitivity reactions, lipodystrophy and anemia).

Antiretroviral syrups, which often have to be used in young children, can be difficult to store. They may require refrigeration. Some households don't have any sort of refrigeration, and even those that do; there may not be enough space to store large quantities of these formulations.

Some ARVs need to be taken with food, so care-givers may have to perform the (often difficult) task of providing a meal and administering drugs simultaneously. This is assuming that an adequate supply of food is actually available.

### **2.2.2 Family/Caregiver Related Challenges**

Adherence to antiretroviral regimens can be particularly daunting for HIV-infected children who often live in families affected by poverty, substance abuse, multiple life stressors and family disruption (Boyd-Franklin *et al.*, 1995), all of which can impair the families' ability to manage the children's illness, including the proper administration of medications.

Due to the stigma surrounding HIV, parents and caregivers are often unwilling to make it publicly known that the child in their care is HIV positive and this can sometimes lead to adherence problems. For instance primary caregiver's may be reluctant to fill out prescriptions in their local community, or may not make a child's school aware of their condition, which can lead to them missing out on drug doses during the schools day. They may also hesitate to administer ARVs if other people are present when a child is due to receive them.

Caregivers are also reluctant to disclose HIV/AIDS to the children. A recent study conducted with caregivers in South Africa reported a 26% disclosure rate among children aged less than six years (Moodley *et al.*, 2006), although all caregivers recognized the importance of pediatric disclosure. Disclosure of HIV or AIDS diagnosis to infected children and youth is indeed a complex process that presents a complex challenge to both families and health care providers (Myer *et al.*, 2006). The HIV-infected parents are reluctant to disclose because they fear 1) its impact on the

child's psychological and emotional health, 2) it may lead to depression in the child, 3) the child cannot keep a secret, 4) the child will suffer from social rejection and stigma (Wiener *et al.*, 1996).

In western Kenya, pediatric caregivers' willingness to disclose a child's HIV status to the child or to other people emerged as key themes related to medication adherence. Assessing caregivers' disclosure and views of disclosure effects are of clear relevance to understanding and monitoring pediatric ART adherence (Vreeman *et al.*, 2008).

Research on family/caregiver variables indicated that children are more likely to adhere if they receive their medication from foster parents rather than biological parents or other relatives (Van Dyke *et al.*, 2002).

The child's relationship with the primary caregiver was also identified as a key factor in medication adherence. Children with a relative or other adult as primary caregiver reported better adherence than those cared for by a biological parent, perhaps because biological parents reveal intermittent adherence difficulties more readily than other caregivers. It is also possible that adherence behavior is more successful in the absence of parental HIV illness and associated psychosocial risk factors. Parental HIV illness may disrupt healthy parenting and adherence behaviors, which place children at increased risk for adverse outcomes (Armistead *et al.*, 1995).

### **2.3 Caregiver Factors Associated With Pediatric Adherence.**

Higher education level of the caregiver showed a positive association with adherence rates. This association was detected by Mellins *et al* (2004), but their sample was

much smaller. This association of education level with adherence has been observed in adults with HIV, along with greater confidence in the benefits of ART (Reynolds *et al.*, 2004, DiMatteo, 2004). The accuracy of care-givers information about the child's HIV medications and corresponding dosages and dosing frequencies has been related to adherence (Katko *et al.*, 2001).

Poverty places families at increased risk for many stressful life events and has been shown to be strongly associated with child non-adherence (Dorsey *et al.*, 1999).

A study of 75 perinatally infected 3 – to 13- years-old in New York, found that non-adherence was related to worse parent-child communication, higher caregiver stress, lower caregiver quality of life, and worse caregiver cognitive functioning (Mellins *et al.*, 2004). The benefit of a positive social support system was also suggested by the higher rates of adherence for participants in the study who used a buddy system to assist them in medication taking. In univariate analysis in a study in West Africa, the major factors related to child non-adherence were: - being female, living in an individual setting (vs. large family compounds), receiving other ART regimen; drug regimes with 6 pills/spoons or more per day; caregiver other than the biological parent; caregiver not declaring HIV-status; not participating to support groups and having perceived difficulty of ARV administration. In multivariate analysis, female gender, living in an individual setting, caregivers perceived difficulty of ARV administration remained independently associated with the reported child's non-adherence. The data showed low rates of perfect adherence to ART in children in West Africa, influenced by child and caregiver characteristics (Julie *et al.*, 2008).

## 2.4 Measurement of Adherence

Further complicating matters is the lack of a "gold standard" to measure adherence across health conditions (Matsui, 2000). A number of clinical and research measurement strategies exist, including pill counts, electronic monitors, diaries, and interviewer-administered or self-report questionnaires (Chesney *et al.*, 2000); yet none are without flaws, and the limitations of these methods are even more pronounced when working with children (Matsui, 2000). For example, not all of the pediatric medications come in pill form and therefore pill counts are often inappropriate. Because caregivers often prepare syringes with correct dosages or pill boxes for the week, Medication Event Monitoring Systems, which record each time a medication bottle has been opened, are often impractical to use clinically or in research studies involving children. Social desirability is the issue most typically associated with self-report questionnaires. In addition, in the case of child adherence, the best source of information is not always clear. Younger children are typically given their medications by a parent, another family member, or other adults (home health aides and school nurses) and may not even know what medications they are supposed to take. On the other hand, as children get older, they may take on more responsibility for managing their medication regimens, and in the transition, the role of the adult changes. Adults may remind the child to take his or her medicine, check medications to determine whether the child appears to be taking them, and/or continue to administer some of the medications themselves. In some cases, adults and children may each have incomplete information on adherence.

Self-reporting by patients and caregivers is, however, one of the methods most commonly employed to measure levels of antiretroviral adherence. Some studies have

compared self-reporting questionnaires with more objective adherence measurements (such as HIV viral levels, CD4 cell count, and plasma antiretroviral count) and found good agreement between self-reporting and objective measurement (Farley *et al.*, 2003).

The appropriate number of days used prior to interview, to measure adherence varies greatly. Measurement of adherence the day before interview is predictive of one's previous month adherence behavior. Weidle *et al* (1998) found that adherence the day before interview is consistent with adherence one month before interview. Those who reported non-adherence the day prior to the adherence interview were 9.9 times more likely to report non-adherence the prior month than those who reported adherence. In another study, the 24RI revealed a high rate of non-adherence. Many children (37%) missed  $\geq 1$  dose of medication over 3 days, consistent with rates derived from electronic monitoring and pharmacy records which suggests that the 24RI may be more successful at measuring when doses are missed (Farley *et al.*, 2003; Watson & Farley, 1999).

## **CHAPTER THREE: MATERIALS AND METHODS**

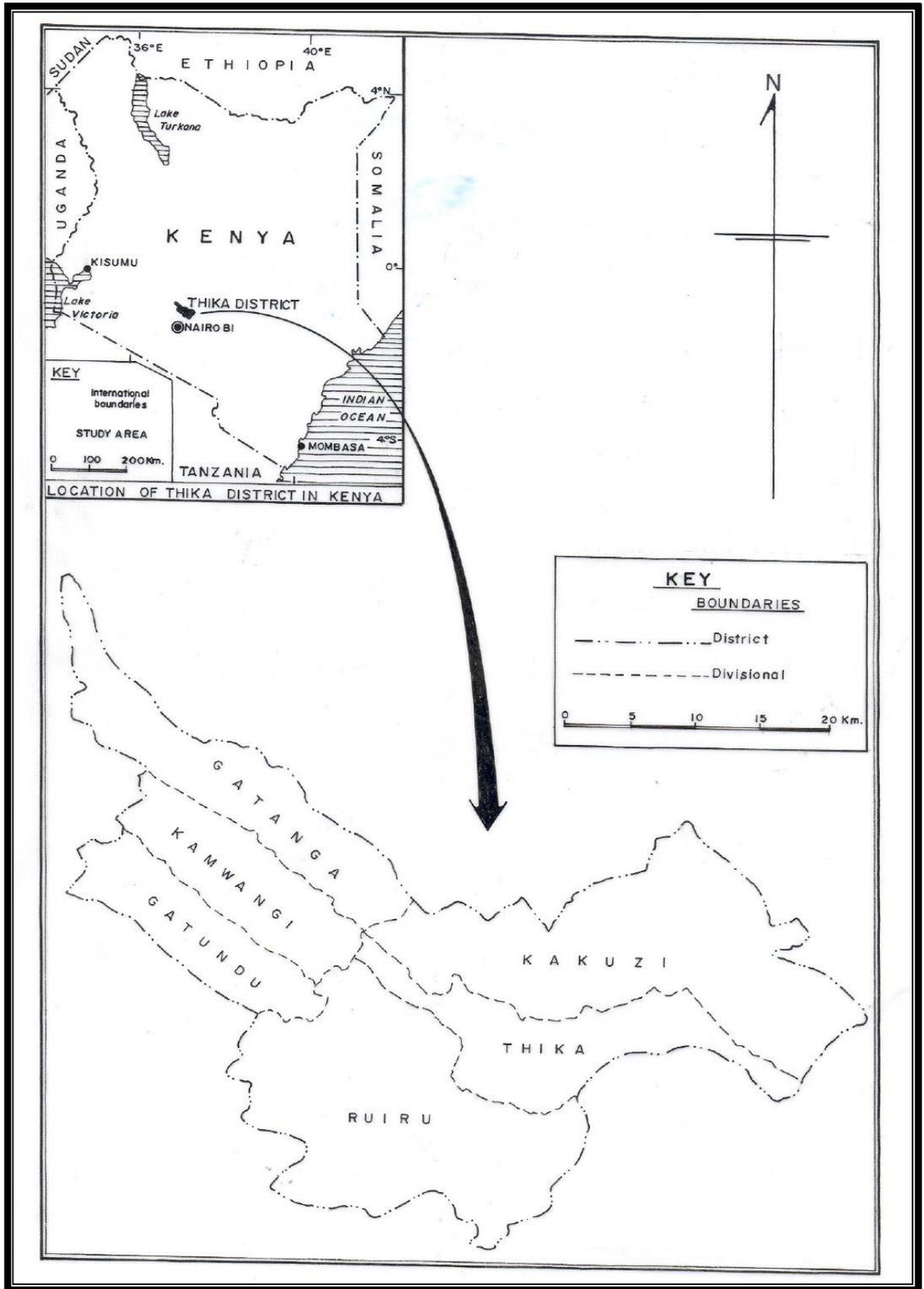
### **3.1 The Study Area**

The Study was carried out at Thika District Hospital, in Thika Town. Thika town is located in Thika District within Central Province of Kenya and is the district administrative headquarters. The town is approximately 47 km north east of Nairobi, at an altitude of between 1420 and 1550 meters above sea level. Thika is one of the satellite towns to Nairobi City.

The population of Thika District according to the 1999 census was 645,713. The municipality had 106,707 persons. The district is predominantly rural, but its urban population is soaring as Nairobi is growing rapidly. The economic activities of the town include agriculture, particularly in the horticulture (exports mainly to Europe) and coffee industry (exports mainly to the USA and Europe). Other industries include textile (cotton), food processing (pineapples, macadamia nuts, and wheat), tannery, motor vehicle assemblies and cigarette manufacturing. About one hundred small scale industries and about twenty major factories exist in and around the town.

Life expectancy is 58 years for women, 53 for men, with a possibility that the figure may have reduced as a result of HIV/AIDS. Central province by end of July 2008 had 1500 pediatric HIV patients. 710 are attended to at Thika District Hospital. Only 231 of the pediatric patients are on ART. However, plans are in place to put all the 710 patients on treatment.

Fig 3.1 MAP OF KENYA SHOWING THIKA DISTRICT



### **3.2 The Target Population**

Kenya, by end of July 2008 had 15090 pediatric HIV patients on ART. The target population comprised all the 15090 primary caregivers of the children on ART.

### **3.3 The Study Population**

Thika District Hospital by December 2008 had 900 pediatric patients on ART. The population of study was the primary caregivers of the 900 children undergoing antiretroviral therapy at Thika District Hospital.

#### **3.3.1 Inclusion Criteria**

Caregivers were considered to be those who report understanding the 24 hour-a day regimen and who are responsible for administering at least 50% of the doses of medication to the child. The sample comprised vertically infected children, from birth to 12 years of age residing in Thika district, who had been reported as AIDS cases, were receiving antiretroviral treatment, and were scheduled for out patient visits between 1<sup>st</sup> December 2008 and 31<sup>st</sup> March 2009.

#### **3.3.2 Exclusion Criteria**

Guardians not responsible for administering treatment and the ones who did not give assent were excluded.

### **3.4 Ethical Considerations**

Approval for the research was sought from the Ethics Committee/Medical Superintendent of Thika District Hospital. The caregivers that agreed to participate signed the Informed Consent Form. The research results were presented in an aggregated form, without identifying the cases included in the study, rigorously obeying the principle of ethics and protecting participant secrecy.

### 3.5 Study Design

The study design was descriptive cross-sectional.

#### 3.5.1 The Sample Size

The sample size was 213 primary caregivers. The formula for sample size determination was  $n = Z^2pQ/d^2$ , where:-

$n$  = required sample size

$Q = 1 - p$

$Z$  = Confidence level at 95% (standard value of 1.96)

$p$  = Estimated prevalence of adherence internationally (20%).

$d$  = level of precision at 5% (Standard value of 0.05)

The sample size was thus:-

$$(1.96)^2(0.2)(0.8) / 0.0025 = 245$$

Since the study population was  $\leq 10,000$ , finite population correction factor was used.

The minimum sample size was:-

$$nf = Nn / N + (n-1) = 900 \times 245 / (900 + 244) = 193.$$

To account for possible drop outs, 10% was added and the actual sample size was 213.

Every patient attending the clinic in the three months were interviewed as long as they met the inclusion criteria.

#### 3.5.2 Sampling Method

Purposive sampling method was used. All primary caregivers bringing the children to the clinic were interviewed as long as they consented to the study.

### 3.5.3 Variables

**The dependent variable** in this study was a qualitative dichotomic “adherence/non-adherence” variable. **The independent variables** consisted of characteristics that hypothetically could influence adherence/non-adherence: age and sex of child, length of antiretroviral treatment; age and sex of the care-giver; caregivers marital status; drug related adherence difficulties; understanding of child’s diagnosis by caregivers and /or professionals at day care/school; if a caregiver has a paying job outside the household; if the caregiver was responsible for taking care of another person(s); presence of HIV in caregiver; use of antiretroviral of caregiver; if the caregiver had difficulty taking antiretroviral; relationship between caregiver and child; caregiver education level/confidence in ART; family income, and stigma/disclosure of HIV status.

### 3.5.4 Study Tools

To measure adherence, a technique was adopted consisting of a structured Interview and a box containing a sample of medications called the medication kit. The data collection instrument consisted of an interview form which was semi-structured into 20 questions, the majority of which were closed, but with some additional open questions (Appendix 1). This instrument brought together data Informed by the caregiver, and the objective data obtained through the medical prescription and from the medical register. The medication kit consisted of a box containing a sample of all the antiretroviral medications used by children up to 12 years old that are distributed by the Ministry of Health. The objective of this tool was to facilitate identification, by the caregiver, of antiretrovirals used by the child, at the moment that he/she was describing the normal administration of these medications to the child.

### **3.6 Logistics of Data Collection and Adherence Verification**

The selection of subjects with criteria for inclusion in the study was based on pediatric clinic records. All caregivers scheduled to visit the clinic in the three months of study were interviewed, with their consent. Children that missed one dose of one medication of the prescribed medicines in the 24 hours period preceding the interview were considered non-adherent. The percentage that missed a dose was calculated, with the numerator representing the number that missed a dose in the previous 24 hour period and the total number interviewed as the denominator. The children were considered adherent if the caregiver recorded giving 100% of the medication in the previous 24 hours prior to the interview.

The team of interviewers consisted of two pharmacy students in their final year of study. Before starting the study the interviewers were given a basic course about the antiretrovirals used to control the AIDS Infection in children, and possible adverse effects, and additional training in interviewing techniques and questionnaire completion. A pilot study was carried out with 10 child caregivers attended by the two interviewers. The test study helped to perfect the questionnaire and to train the team of interviewers. The responses given by the caregivers included in the pilot study were not included in the sample.

### **3.7 Data Analysis**

The completed questionnaires were coded; data entered; cleaned and processed using SPSS 12.0 (SPSS Inc Chicago USA) statistical packages. Descriptive statistics were run to explore the rate of adherence, the socio-demographic characteristics of the caregivers and children, the socio-economic/ socio-cultural characteristics of the

caregivers and the drug related adherence difficulties experienced by the caregivers. The significance of the association between the diverse independent variables and outcome occurrence (adherence/non-adherence) was estimated by utilizing Pearson's chi-square test with 95% (95%CI) confidence interval. To adjust for the effect of confounding variables multivariate analysis (logistic regression) was utilized using STATA version 9.0. The multivariate equation used was as below:-

$$\text{Adherence} = \beta_0 + \beta \text{ Age} + \beta \text{ Gender} + \beta \text{ mstatus} + \beta \text{ Edu} + \beta \text{ Rlship} + \beta \text{ Estatus} + \varepsilon$$

Adherence was a function of primary caregivers' age, gender, marital status, level of education, relationship to the child, employment status and the error margin. The level of significance adopted in the bivariate and multivariate analysis was 0.05.

## CHAPTER FOUR: RESULTS

### 4.1 Estimate of Adherence/Non-Adherence

The final sample consisted of 200 caregivers with a response rate of 93%.

57.5 % (115) of the caregivers admitted to having missed a dose of at least one medication in the past 24 hours. This puts the estimated rate of non-adherence at 57.5%. The rate of adherence at Thika District Hospital, therefore, was 42.5 % with 85 respondents having taken 100% of their medication the previous day. At 95% confidence interval the adherence rates will vary between 35.65% and 49.35% (Table 4.1).

**Table 4.1 Caregivers reported prevalence of adherence to HAART among children at Thika District Hospital.**

Variable	Frequency	Percentage
Missed a dose of a medication in the last 24 hours.		
Yes	115	57.5
No	85	42.5

**PREVALENCE OF ADHERENCE 42.5% (95% CI 35.65% - 49.35%)**

## **4.2 Factors Associated With Adherence to Art Bivariate Analysis)**

### **4.2.1. Association of Adherence to Socio-Demographic Characteristics of the Caregiver and Child**

#### **4.2.1.1 Gender of the Caregiver**

Majority (122) of the respondents were female representing 61 %. 40% of the female compared to 46% of the male caregivers' adhered to medication, while 60% of the female compared to 54% of male caregivers' did not adhere to the ARV medication. The variable "sex of the caregiver" showed no significant statistical importance to adherence. ( $\chi^2=0.699:1df: p>0.05$ ) (Table 4.2)

#### **4.2.1.2 Age of the Primary Caregiver**

The mean and median age of the caregivers was 38 and 37 years respectively. Majority of the caregivers (27%) were between 31 – 40 years, followed by those in the 41 – 50 age brackets (21%). The lowest percentages of adherence were observed in caregivers 20 years of age and below (32%) and those above 60 years (31%). There was no statistical significance association between age of the primary caregiver and adherence ( $\chi^2=4.495:5df: p>0.05 [0.481]$ ) (Table 4.2)

#### **4.2.1.3 Marital Status of the Primary Caregiver**

104(52%) of the caregivers were single. They were either widows/widowers, divorced or were unmarried. 96(48%) were married or living with a partner. 43% of both the married and single caregivers' did adhere, while 57% of both married and single caregivers' did not adhere. Caregivers' marital status however showed no statistical significant association to adherence to ART in children at Thika District Hospital ( $\chi^2=0.006:1df: P>0.05$ ). (Table 4.2)

#### **4.2.1.4 Relationship of the Primary Caregivers to the Child**

78 % ( 157) of the children were being cared for by their biological parents, 17% (34) by their guardians while 5% (9) were under foster care. A lower rate of adherence was observed among parent caregivers compared to guardians/foster parents. Caregivers' relationship to the child was independently associated with adherence with a p value of 0.018 (Table 4.4).

#### **4.2.1.5 Gender of the Child**

A hundred and twelve (56%) of the children were female and 88(44%) were male. As observed in table 4.5, there was adherence among 44.5% of male compared to 40% of female children. There was no statistical significant association between adherence and gender of the child ( $\chi^2 = 0.37; 1df; p > 0.05$ ) (Table 4.2).

#### **4.2.1.6 Age of the Child**

Majority, 115(57.5%) were over 5 years, 85(42.5%) were under 5. Children under 5 years of age recorded the lowest percentage adherence cases (38%). Age of the child had no association with adherence. ( $\chi^2 = 1.10; 1df; p > 0.05 [0.233]$ ) (Table 4.2).

**Table 4.2 Association of Adherence to Socio-demographic Characteristics of Caregiver and Child**

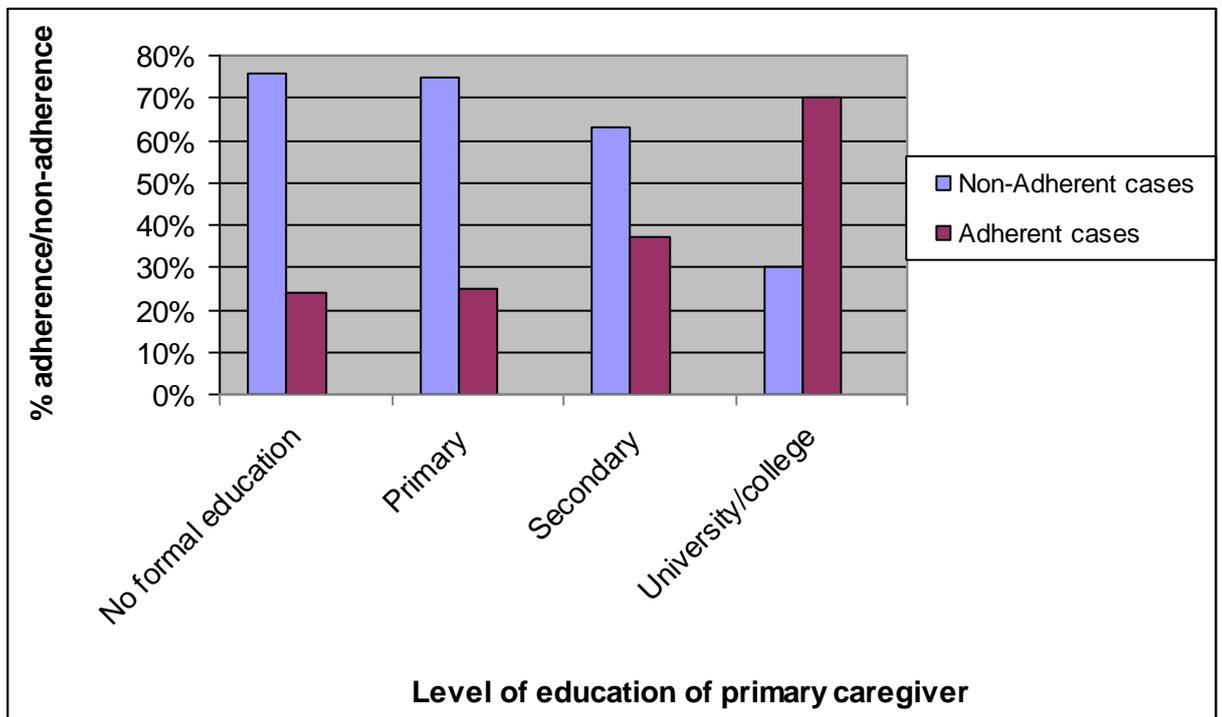
<b>Independent Variable</b>	<b>Frequency (n)</b>	<b>Adherent (n)</b>	<b>Non-Adherent (n)</b>	<b>Statistical Test</b>
<b>Sex of care giver</b> Male Female	73(39%) 122(61%)	46.2%(36) 40.2%(49)	53.8% (42) 59.8%(73)	$\chi^2=0.699:1df$ : $P>0.05$ [0.403] <b>not significant</b>
<b>Age of care giver</b> 20 and below 21 - 30 31 - 40 41 - 50 51 - 60 61 and above	25(12.5%) 35(17.5%) 53(26.5%) 42(21%) 29(14.5%) 16(8%)	32% (8) 40% (14) 47.5% (25) 40.5% (17) 55.2% (16) 31.2 (5)	68% (17) 60% (21) 52.8% (28) 59.5%(25) 44.8% (13) 68.8 %(11)	$\chi^2=4.495:5df$ : $P>0.05$ [0.481] <b>not significant</b>
<b>Marital status of caregiver</b> Single Married	104(52%) 96(48%)	(43%)45 (43%)41	(57%)59 (57%)55	$\chi^2=0.006:1df$ : $P>0.05$ [0.936]: Yates corrected. <b>not significant</b>
<b>Caregivers relationship to the child</b> parent Guardian Foster care.	157(74%) 34(17%) 9(5%)	62(40%) 19(56%) 4(44%)	95(60%) 15(44%) 5(56%)	$\chi^2=3.096:3df$ : $P>0.05$ [0.018]: <b>significant</b>
<b>Sex of the child</b> Male Female	88(44%) 112(56%)	45.5%(40) 40.2%(45)	54.5%(48) 59.8%(67)	$\chi^2=0.37:1df$ : $P>0.05$ [0.454]: Yates corrected <b>not significant</b>
<b>Age of the child.</b> Under 5 years Over 5 years	85(42.5%) 115(57.5%)	37.6%(32) 46.1%(53)	62.4%(53) 53.9%(62)	$\chi^2=1.10:1df$ : $P>0.05$ [0.233]: Yates corrected <b>not significant</b>

## 4.2.2 Association of Adherence to the Socio-Economic Characteristics of The Caregivers (Bivariate Analysis)

### 4.2.2.1 Education Level of the Primary Caregivers

Twenty one (11%) of the caregivers had no formal education, 44 (22%) had primary education, 71 (36%) had attained secondary level of education, 64(32%) had university education. There was a statistically significant association between the variables “caregiver’s education level” and adherence with  $p < 0.05$  ( $\chi^2 = 15.3: 4df$   $p = 0.001$ ) in bivariate analysis (Table 4.3). Adherence rates increased with increased primary caregivers’ level of education (Fig 4.1).

**Fig 4.1:- Relationship between adherence/non-adherence and caregivers education level**



#### 4.2.2.2 Employment Status and Average Monthly Income of the primary caregivers'

One hundred and sixty four (82%) of the caregivers were in employment (formal/informal) while 36(18%) were unemployed. Caregiver's source of income was not statistically associated with adherence ( $\chi^2=6.47:1df$ :  $p>0.05$ ). It was however, noted that a lower proportion of those in employment adhered to ART (Table 4.3)

The average monthly income was 87\$ with a median of 99\$ and a standard deviation of 67\$ and average monthly income ( $\chi^2=5.866:3df$ :  $p>0.05$ ) did not show a significant association with adherence/non-adherence (Table 4.3).

**Table 4.3:- Association of adherence to Socio-economic characteristics of the caregivers**

<b>Independent Variable</b>	<b>Frequency (N)</b>	<b>Non-Adherent (N)</b>	<b>Adherent (N)</b>	<b>Statistical Test.</b>
<b>Caregivers education level</b>				$\chi^2=24.056:3df$ : $p<0.05$ [0.001] significant
Lack of formal education	21(10.5%)	76%(19)	24%(6)	
Primary	44(22%)	75%(33)	25%(11)	
Secondary	71(35.5%)	63%(45)	37%(26)	
University/college	64(32%)	30%(18)	70%(42)	
<b>Caregivers source of income</b>				$\chi^2=6.47:3df$ : $p>0.05$ [0.094] not significant
Employed	164(82%)	59%(96)	41%(68)	
Unemployed	36(18%)	50%(18)	50%(18)	
<b>Caregivers average monthly income.</b>				$\chi^2=5.866:3df$ : $p>0.05$ [0.118] not significant
< 63\$	94(47%)	56.4%(53)	43.6%(41)	
63\$-125\$	64(32%)	67.2%(43)	32.8%(21)	
126\$-187\$	23(11.5%)	39.1%(9)	60.9%(14)	
188\$ and above	19(9.5%)	47.4%(9)	52.6%(10)	

### **4.2.3 Socio-Cultural Characteristics, Knowledge and Perception of Art**

#### **4.2.3.1 Knowledge and Perception Of Art**

100% of the caregivers approved the use of ART and were willing to continue administering the medication. However, only 77% knew that ARV's reduced the progression of HIV. 23% either believed it was a cure, meant for pain relief or had no idea of the role played by ARV's. 92 % ( 184) of the caregivers were able to identify the drugs the children were taking. 16% could not identify the medication.

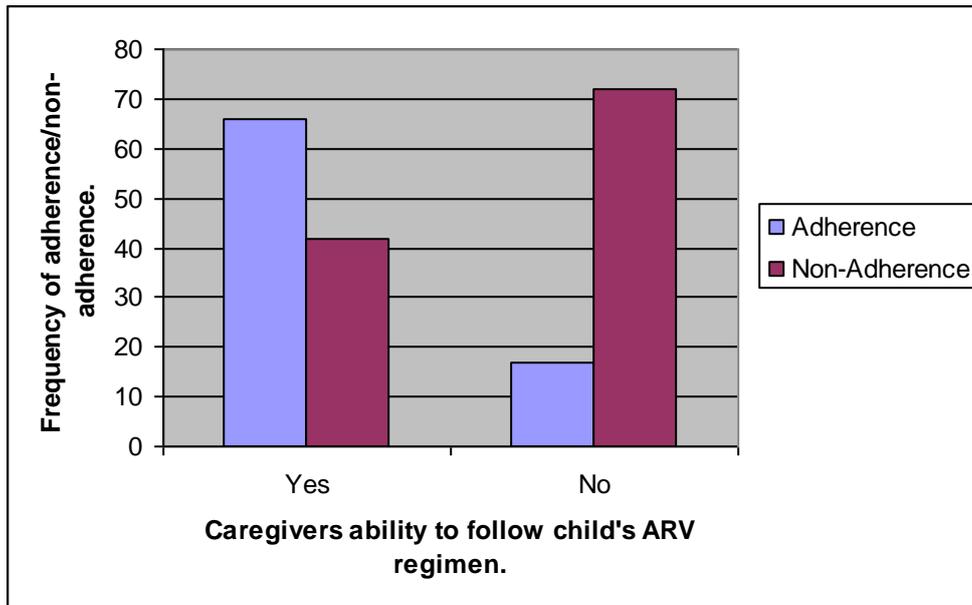
100% of the caregivers admitted to having observed benefits from the child's use of ART with 6% recording weight gain, 30% observed normal healthy growth while 64% had observed reduced incidences of ill health (Table 4.5)

A hundred and eight (54.8%) of the caregivers were able to follow the child's ARV medication, while 89(45.2%) were not able to follow the child's ARV medication (Table 4.5). As observed in table 4.6, the caregivers ability to follow the child's ARV medication showed a statistically significant association with adherence ( $\chi^2=35.31:1df: p<0.05$ ). Majority of the caregivers who were able to follow the child's ART treatment adhered to medication, while a significant majority of those who were unable to follow the child's ART medication did not adhere (Fig 4.2).

**Table 4.4 Distribution of Caregivers Knowledge and perception of ARV drugs**

<b>VARIABLE</b>	<b>FREQUENCY (N)</b>	<b>FREQUENCY (%)</b>
<b>Role of ART.</b>		
Reducing progression of HIV	154	77
Curing HIV	12	6
Reducing pain	20	10
Don't know	14	7
<b>Benefits of ART</b>		
Weight gain	12	6
Normal Health	60	30
Reduced ill Health	128	64
<b>Ability to follow ART</b>		
Able to follow	108	54.8
Unable to follow	89	45.2
<b>Duration on treatment</b>		
less than 5 years	164	82.0
over 5 years	36	18.0
<b>Co- treatment</b>		
On other medication	131	65.5
Not on other medication	69	35.5
<b>Parents and ART</b>		
On ART	110	67.9
Not on ART	52	32.1

**Fig 4.2:- The relationship between Caregivers ability/inability to follow child's ARV regimen with adherence/non-adherence**



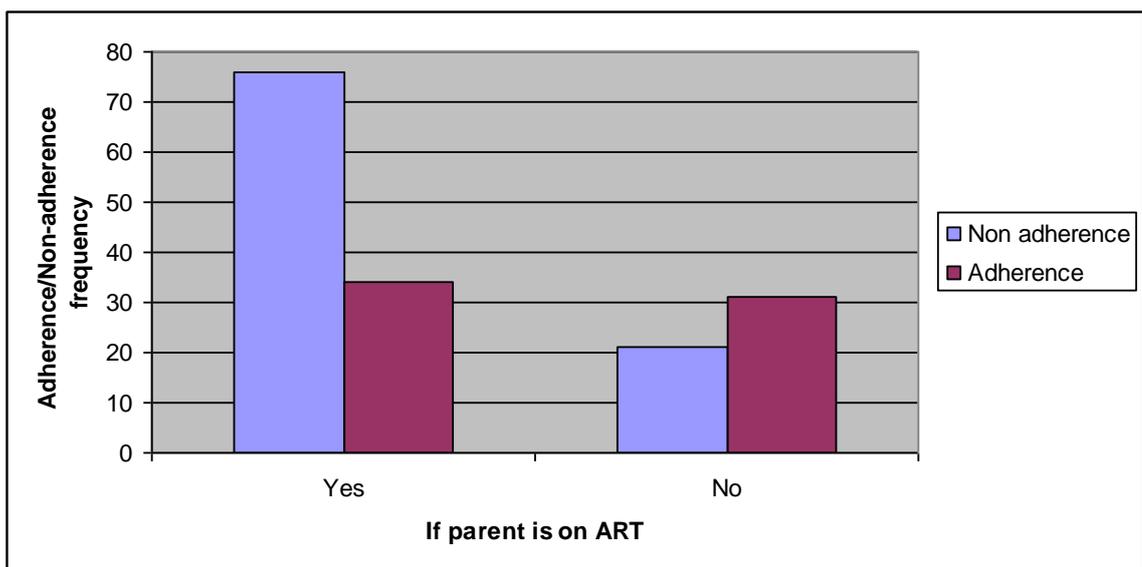
Those not able to follow the child's ART admitted to having problems administering every dose of the ART to the child everyday. The problems cited included "Busy schedules that forced them to be out thus missing a dose, forgetting to administer the medication, lack of assistance from other family members, child's refusal to take medication"

A high percentage of children (65.5%) were on other medications, however only 23.7% of their caregivers' believed that it affected administration of the ARV.

Majority (164) of the children had been on ART for less than 5 years (Table 4.5). The length of time the children had been on ART showed no significant association with adherence ( $\chi^2=0.850:1df: p>0.05$ ) (Table 4.7).

110 parents were on ART therapy, while 52 had not yet been put on medication (Table 4.5). The fact that parents were on ART was significantly associated with adherence ( $\chi^2=12.111; 1df; p<0.05$ ) (Table 4.7).

A significant proportion of parents on ART had problems with adhering to the child's ART, while a higher proportion of the parents not on medication adhered to the child's ART (Fig 4.3).



**Fig 4.3 Frequency of Adherence/Non- Adherence among Parents on ART**

81(73.6%) of the primary caregivers admitted to having difficulty adhering to own medication. There was a statistically significant association between caregivers difficulty in adhering to own ARV medication” and child’s adherence/non-adherence outcome with a  $p<0.05$  (Table 4.7).

#### **4.2.3.2 Socio-Cultural Factors**

40.7% (47) of the children over 5 years of age were aware of their status, while 53% (68) were not aware of their status. 51% of those who are aware of their status

adhered to medication, while 53.6% of those not aware adhered to their medication. The child's knowledge of HIV status had no significant association with adherence/non-adherence outcomes ( $\chi^2=0.01:1df: p>0.05$ ) (Table 4.7). Out of the 101 children attending school, only 16(15.8%) of the caregivers were willing to inform the teachers of the child's status. 85(84.2%) caregivers were unwilling to share the information with the teachers. All the 101 caregivers believed that disclosure would have no effect on adherence (Table 4.6).

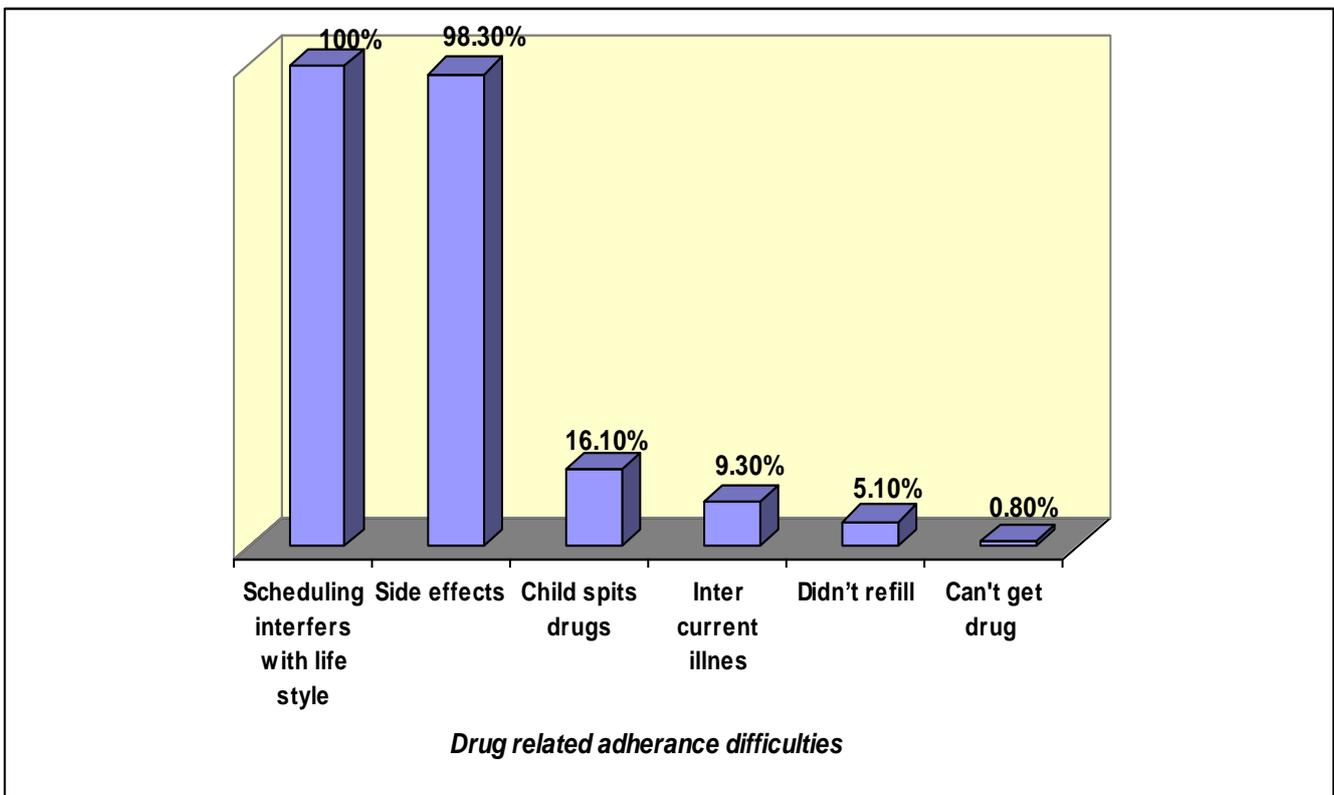
**Table 4.5: Association of Caregivers' Knowledge and Perception of ART to Adherence**

Variable	Adherence		Statistical Test
	Non Adherence (n)	Adherence (n)	
<b>Ability to identify drugs the child is on.</b> Yes No	<b>57.1%(105)</b> <b>62.5%(10)</b>	<b>42.9%(79)</b> <b>37.5%(6)</b>	$\chi^2=0.03:1df: p>0.05$ [0.874];Yates corrected <b>not significant</b>
<b>Drug related difficulties/Problems administering ART to the child.</b> Yes No	<b>80.5%(95)</b> <b>17.4%(20)</b>	<b>19.5%(23)</b> <b>72.9%(62)</b>	$\chi^2=60.07:1df: p<0.05$ [0.0001;Yates corrected <b>significant</b>
<b>If able to follow child's ARV regimen</b> Yes No	<b>39%(42)</b> <b>81%(72)</b>	<b>61%(66)</b> <b>19%(17)</b>	$\chi^2=35.31:1df: p<0.05$ [0.0001;Yates corrected <b>significant</b>
<b>If parent is on ART</b> Yes No	<b>69%(76)</b> <b>40%(21)</b>	<b>31%(34)</b> <b>60%(31)</b>	$\chi^2=12.111:1df: p<0.05$ [0.001]; Yates corrected <b>significant</b>
<b>Caregiver's difficulty in Adhering to own ARV medication.</b> Yes No	<b>82%(73)</b> <b>48.3%(14)</b>	<b>18%(16)</b> <b>51.7%(15)</b>	$\chi^2=11.18:1df: p<0.01$ [0.001;Yates corrected <b>significant</b>
<b>Child's knowledge of ARV status</b> Aware Not aware	<b>51%(25)</b> <b>53.6%(37)</b>	49%(22) 46.6%(31)	$\chi^2=0.01:1df: p>0.05$ [0.927];Yates corrected <b>not significant</b>
<b>Duration on ART</b> Less than 5 years Over 5 years	<b>55%(91)</b> <b>64%(23)</b>	45%(73) 36%(13)	$\chi^2=0.850:1df: p>0.05$ [0.232]; Yates corrected <b>not significant</b>

#### 4.2.4 Drug Related Adherence Difficulties

100% of the caregivers agreed that scheduling of the drug administration interfered with lifestyle (school, work and food) while 98% agreed that side effects were a problem. 16.1% of the children spit the drugs as a result of the taste. 9.3% of the children had inter-current illnesses that interfered with drug administration. Only 5.1% did not get the drugs refilled at the right time while 0.8% could not get the relevant drug (fig4.4).

**Fig 4.4 Drug related Adherence Difficulties among primary caregivers**



### 4.3 Caregiver Factors Associated With Adherence To Art (Multivariate Analysis)

The level of education of primary caregiver and caregiver relationship to the child emerged to be true predictors of pediatric ART adherence. The resulting model is tabulated below,

#### Case definition

Dependent Variable: - Adherence =1 Non-Adherence= 0

Independent Variables: Age (Below 18 = 0 above 18= 1), Gender (Female = 1 male = 0), Marital Status (single = 0 married = 1), Education level (with formal education = 1 without formal education = 0), relationship to the child (Parent = 0 Guardian = 1), Employment status (Unemployed = 0 Employed = 1)

**Table 4.6:- Logistic Regression predicting primary caregivers' age, gender, marital status, relationship to the child, and education level and employment status by adherence outcomes at Thika District Hospital**

VARIABLE	WALD	PVALUE
Gender of the caregiver	0.457	0.499
Age of the caregiver	0.001	0.981
Marital status of the caregiver	0.014	0.907
Caregivers' relationship to the child	5.588	0.018
Caregivers' education level	7.995	0.005
Caregivers' employment status	2.120	0.232

## CHAPTER FIVE:-DISCUSSION, CONCLUSION AND RECOMMENDATIONS

### 5.1 Discussion

This study found an estimated prevalence of adherence to antiretroviral treatment in children residing in Thika district of 42.5%. Only 42.5% of the caregivers administered 100% of the medication in the 24 hours preceding the interview. This is comparable to findings in West Africa, with 42% of the caregivers declared perfect adherence, 58% did not adhere to the ART (Julie *et al.*, 2008). A study in Brazil estimated the prevalence of adherence to ARV treatment in children living in Porto Alegre of 49.5%. The prevalence of non-adherence in this study(57.5%), was higher than that in international studies, as non-adherence in children, analyzed in international studies, showed prevalence of 30% (Van Dyke *et al*, 2002).

As there is no gold standard of measuring adherence as well as the fact that adherence classification cutoff point may not be perfect in different setups, the results cannot be compared or contrasted.

This study showed no significant association between the caregivers' "gender" with adherence. A slightly higher percentage of male caregivers, however, showed more adherent cases than the female. This can be explained by the fact that even when married, the burden of running the home is most often on the woman's shoulder. Women are thus overburdened with responsibility and where there is no support, can easily forget to administer treatment to the child. Where the women are single and have the additional task of fending for the family, the risk of non-adherence is high. Women thus whether single or married have difficulty coordinating adherence with work, family or care giving responsibility. These results compare with a study in

West Africa related being a female caregiver to child non-adherence (Julie *et al.*, 2008).

Caregivers' age was not associated with adherence. It was however observed that prevalence of adherence was low among caregivers below 20 and those over 60 years of age. These have low capacity or low ability to adhere, as adherence is dependent on having the necessary cognitive and technical skills to follow a medication scheme, perceived self efficacy and problem solving capacity. The caregivers' age can be used as a guide to assess their ability to follow the child's treatment.

There was no difference in adherence between those married and those living single. It is assumed that if married, caregivers should be able to cope with ART administration as responsibility for drug administration is shared. Adherence prevalence should be higher among the married caregivers'. This was however not the case in this study. The caregivers' marital status did not affect adherence.

"Caregivers' relationship to the child" was independently associated with child adherence in this study. Children cared for by guardians had a slightly higher prevalence of adherence. One of the explanations of this observation could be that the guardians were more committed to giving the children medication because they readily and willingly accepted the responsibility of the child's care, thus the child was not a burden to them. Higher prevalence of non-adherence would be observed in cases where the child was a burden to the guardian, who in this case, could be a relative that possibly has taken over the care of the child more because of the imposition of a situation, such as advanced AIDS or death of the biological parents, than of his/her

own free will. It is thus important that the team that treats the child be aware of the quality of the relationship between the caregiver and the child, and should involve other family members in the management of the child's disease where necessary. There was no protection against non-adherence for children in foster care in this study. Other researches on family/caregiver variables have, however, indicated that children were more likely to adhere if they received their medication from foster parents than from biological parents or other relatives (Muller *et al.*, 2007). Muller concluded that all the children in foster care recorded good adherence within the 24 hour schedule. Of importance is that those under the care of parents registered low prevalence of adherence in this study. Biological parents in these cases are definitely infected with HIV, and they experience psychological and physical health complications. Parental HIV illness disrupts healthy parenting which place children at increased risk for adverse outcomes. Often a good number are on medication and find it difficult to adhere to their medication. Biological parents may also be more likely than other caregivers to also be of lower socioeconomic status, thus reducing chances of adherence as stress levels are higher. Parents with HIV disease may require increased social support to ensure medication success for their children, particularly if their current or chronic life stress is high (Bauman *et al.*, 2007).

A higher prevalence of adherence was observed among the male children. Sex of the child did not show any association with adherence. Children under 5 years of age recorded lower adherence prevalence compared to those over 5 years of age. Children under 5 years of age pose a challenge to adherence as they are known to spit the drug especially if unpalatable, or simply refuse to take medication; sleep patterns can also interfere with administration of medication. There was, however, no statistically

significant association between adherence and “age of the child”. This concurs with a study conducted in Brazil, where the same characteristics were shown not to be associated with adherence/non-adherence (Naiva *et al.*, 2006). Some studies have, however, suggested that older children are more likely to be non-adherent, (Reddington *et al.*, 2000; Arrive *et al.*, 2005).

Aspects related to treatment such as “duration of treatment” and “whether the child was on other medication” were of no significance in as far as adherence is concerned at Thika District hospital. A study in Brazil also showed that the “time of use” and “number of drugs composing the therapeutic regimen” had no relationship with non-adherence (Naiva *et al.*, 2006). Despite these findings, however, healthcare givers should take into consideration the pharmacokinetics and pharmacodynamic factors of the drugs. Such issues as; need for daily administration, dietary restrictions, drug interactions, frequency of dosing, dosage and pill burden or amount of liquid will influence child’s adherence to therapy (<http://AIDSinfo.nih.gov>). In order to improve adherence, possible regimens should be simplified with respect to number of pills or volume of liquid prescribed and frequency of therapy. Adherence is often enhanced by changing from a thrice daily dosing schedule to twice daily; when the pill burden is too great for a child, provide a regimen maintaining fewer pills. Formulations having less dietary restrictions and less drug interactions will be helpful in improving adherence. The simpler the regimen and administration, the less the frustration to the caregiver and the better the chances of adherence.

This study suggests that better caregiver education is associated with adherence in a bivariate analysis. Better caregivers’ education was independently associated with

better adherence. The failure to find an association with caregivers' ability to describe a regimen and adherence suggests that it is the caregivers' overall education that impacts more on the treatment adherence than literacy per se. Orrell *et al.*, (2003) also concluded that better caregivers' education was strongly independently associated with better adherence. Higher caregiver education level has also been associated with adherence among the youth (Williams *et al.*, 2006). The level of education is an important indicator of one's cognitive and technical skills.

The caregivers' economic status in this study had no association with adherence/non-adherence. However, it was observed that majority of the caregivers who had difficulty adhering to medication were in the lowest income level, with those in the highest income levels displaying high adherence prevalence. Orrell *et al.*, (2006) concluded that better caregiver socio-economic status was strongly associated with adherence. Poverty has been shown to place families at increased risk for many stressful life events and has been shown to be strongly associated with child non-adherence (Dorsey *et al.*, 1999).

It has been noted that caregiver's HIV positive status was a predictor of non-adherence (Mellins *et al.*, 2003). Adherence behavior was more successful in the absence of parental HIV illness. In this study, majority of the parents (70%) were on ART and there was significant association between this variable and adherence outcome in the bivariate analysis. When subjected to multivariate analysis, the same variable was shown not to be independently associated with non-adherence. In a study carried out by Gibb *et al.*, (2003) in which it was investigated whether the caregiver used antiretrovirals or not, the authors found no significant association with this

variable and non-adherence. The fact that the caregiver is seropositive and on ARV is not a predictor of non-adherence outcomes.

In this study, 59% of the caregivers on ART, admitted to having difficulty adhering to own ARV medication. Their difficulty in adhering to own medication was associated with non-adherence outcomes in the children in bivariate analysis and was however not a predictor of non-adherence in multivariate analysis. Therefore according to this study, the fact that caregivers found it difficult to adhere to own medication, does not affect administration of ART to the child. Healthcare providers should however monitor caregivers own adherence, identify and address the specific barriers to adherence, encourage and educate them on the relevance of adherence to ARV medication.

The accuracy of caregivers' information about the Child's HIV medication and corresponding dosages and dosing frequencies has been related to adherence (Katko *et al.*, 2001; Marhefka *et al.*, 2004). Parents of adherent children report higher perceptions of their ability to administer the prescribed dose and of the medication efficacy (Wrubel *et al.*, 2003). Ability, in this case depends on the caregivers' cognitive and technical skills to follow a medication scheme. This requires accuracy of information about the child's medication, dosage and dosing frequency. Caregivers' ability to follow the ARV regimen is of significance in maintaining high adherence levels. A good number of caregivers in this study had good knowledge of the child's regimen and could all identify the drugs the child was on. Those who were able to follow the regimen showed more adherent outcomes while those who were not able to follow the regimen had high non-adherent outcomes. Therefore any caregiver who is unable to follow the child's ARV medication/ regimen irrespective of their,

age, marital status, economic status, should not be expected to adhere to the child's medication. Information about the child's HIV medication, dosages and dosing frequencies should be very clearly understood. The caregivers' cognitive factors should be put into consideration. Since ARV treatment is rarely an emergency, time should be invested in preparing the caregiver. If need be the healthcare providers should admit the child until such a time when they will be confident of the caregivers accuracy of the stated information and ability to administer the treatment successfully.

It is notable in other studies that nearly 40% of caregivers experience problems with giving ART and this has adversely affected adherence. Scheduling treatment with lifestyle was the most commonly reported problem. (Gibb *et al.*, 2003; Van Dyke *et al.*, 2002). In this study, 59% of the caregivers admitted to having problems administering ART to the children. The problems were largely drug related. All the 59% were in agreement that scheduling of the treatment interfered with lifestyle, with 57% citing side effects as an additional reason. Non adherence was associated with caregivers' perceived difficulties administering ART to the child. Treatment should therefore be tailored for each patient. The regimen should match child's or family lifestyle and daily schedule as this will help improve adherence. Education on expected side effects and how to possibly combat the same will go a long way in enhancing pediatric drug adherence.

One of the entry points that complicated the issue of adherence for HIV infected children is the issue of disclosure of HIV status to the child (Mellins *et al.*, 2003). In this study only 39 % ( 47) of the children over 5 years of age were aware of their disease. Among the 61% (68) who were not aware, 73.5 % ( 50) of the caregivers were

willing to inform the children. They however did not believe the knowledge would affect ARV administration. This study showed no association between child's knowledge of HIV status and adherence ( $p>0.05$ ). Other studies have also showed no effect of disclosure on adherence to ART (Gibb *et al.*, 2003; Reddington *et al.*, 2000). With increased survival, one of the greatest psychosocial challenges that parents and caregivers of perinatally HIV-infected children face is disclosure of HIV serostatus to their infected children. HIV diagnosis disclosure entails communication about a potentially life threatening, stigmatized and transmissible illness and many caregivers fear that such communication may create distress for the child. Disclosure of a child's HIV diagnosis often leads to disclosure of other family secrets, including paternity, and parental history of sexual behavior and substance abuse. Thus, not only are parents' decisions to disclose affected by their fears about the emotional consequences of disclosure for the child, but also their fears about the child's anger towards the parent, and the potential social consequences associated with the child sharing the diagnosis with others (ostracism, negative reactions from family, friends and school, lack of community support). Many families' are thus reluctant to discuss the nature of the illness with their infected child or adolescent, yet delays in disclosure of HIV infection may potentially result in negative consequences. Lack of disclosure may impair treatment understanding and participation and increase psychological and behavioral problems (Leicester *et al.*, 2002). As children reach adolescence and begin risk-taking behaviors, knowledge about their disease becomes essential for both personal health maintenance and HIV prevention within the larger population.

Studies have shown that complete parental disclosure helps to motivate HIV-infected children to adhere to their daily medical regimen. Disclosure enables children to

understand HIV infection and to make sense of disease-related experiences and the importance of adherence (Waugh, 2003; Balsini *et al.*, 2004). A study in Uganda identified complete disclosure as a factor related to good adherence (Bikaako-Kajura *et al.*, 2006). Another study by Polliset *et al.*, (2009), also revealed that disclosure of HIV status to children over 6 years of age and involving children in the decision-making process regarding therapy modifications has been reported to enhance the child's cooperation with treatment. Published rates of disclosure among pediatric population are widely varied, ranging from 18% to 77% (Lester *et al.*, 2002). There is a strong recommendation from the American Academy of Pediatrics that children and adolescents with HIV be told their diagnosis. There is however need to assess the nature of the parental relationship and consider support activities aimed at caregivers on how to announce the serological status to the child (Weiner *et al.*, 2007). A more comprehensive understanding of the effect of HIV disclosure on Quality of Life is important for developing appropriate strategies for disclosure to children and adolescents with HIV. Concrete guidelines should be provided to support healthcare providers and families in the process of disclosure.

Reluctance to disclose the child's status to the teachers and other members of the family has a negative effect on adherence. Stigma is therefore still an issue in HIV drug adherence. Much as disclosure to teachers did not have any significant relationship to adherence outcomes in this study, very few parents were willing to disclose the child's status to the teachers. They believed that this will not affect non-adherence in any way. According to Wrubel *et al.*, (2005), parents of adherent children report less concern about others discovering their child's diagnosis. Disclosure should be encouraged, not only to teachers in school but also to the

extended family members. This will eliminate the issue of children missing doses because they are in school or reluctance to administer treatment because there is a visitor. There is need for increased knowledge and awareness of HIV disease targeting stigma, with the aim of incorporating the family and community in the management of pediatric HIV.

The perception and belief in the efficacy of treatment, knowledge of the disease and cART have been identified as significant predictors of child adherence (Polliset *et al*, 2009). A change in health status has also been identified as a relevant issue in relation to adherence to cART in pediatric patients (Giacomet *et al.*, 2003). Caregivers' good ability to identify the drug the child was on, their knowledge on the role of ARV, their 100% approval of ART and observed benefits to ART administration are good indicators of possible adherence improvement in this study. There is need to however for continual assessment of regimen knowledge at periodic intervals to identify families at risk for non adherence so that educational interventions can be tailored toward this group (Myung *et al.*, 2007).

This study had some limitations and strengths. The main limitation of this study was recall bias. In this study, adherence prevalence was measured using self-reports from the caregivers, which tends to overestimate the prevalence of adherence. Caregivers might be prone to social desirability bias responding inappropriately to the research assistants. The cross-sectional nature may hinder the ability to exactly identify the predictor of adherence, unlike a longitudinal design. There is no gold standard assessment of adherence. Adherence classification cutoff points may not be perfect in different setups to compare and contrast the findings. Despite the above limitations,

the study had several strengths, including using a relatively large sample size and correct method of data analysis.

## **5.2 Conclusion**

This study shows that adherence to ART at Thika District Hospital is definitely a challenge, given the low prevalence of adherence. It is concluded that the majority of caregivers in this setting are unable to attain optimal adherence (taking <95% of the doses of the combination every week). Less than 95% adherence rates is associated with virologic failure of 75% and increases the risk of drug resistance.

Much as lifelong adherence to complex medication regimens in pediatric ART is an extremely difficult task, it is important for the healthcare providers to take note of the possible predictors and risks to ART adherence at Thika District Hospital, in a bid to increase adherence rates in the District.

The age, gender, marital status, economic status of the caregivers at Thika District did not show any meaningful association with adherence. The gender, age of the child under care, duration of treatment and number of drugs taken by the child were also not of importance in as far as adherence is concerned.

The ability of the caregiver to follow ART regimen which was based on understanding of the dosage/dosing schedules of the drug was positively associated with adherence in bivariate analysis. Family caregivers with thorough understanding of the regimen, accurate information about the Child's HIV medication, corresponding dosages, dosing frequencies and are able to follow the treatment show better adherence to ART.

As long as caregivers have perceived/real drug related difficulties administering ART to the child everyday, adherence will not be attained. . Drug administration interfering with lifestyle/daily activities was associated with adherence in bivariate analysis.

Higher caregiver education is positively and independently associated with adherence. The caregivers' education level is therefore a predictor of adherence. The higher the education level, the higher the rates of adherence.

The nature of the child–caregiver relationship was also independently associated with adherence and is a predictor of adherence. Adherence rates are higher when children are taken care of by guardians or foster parents. Children under the care of their parents show low adherence rates to ART. There is thus need for social support to the parents and inclusion of other members of the community in the management of the child with HIV.

There is need for education and information on HIV in the community aimed at changing the attitude and facilitating acceptance within communities. This will de-stigmatize HIV disease, enhance disclosure, and facilitate mobilization of the needed social support with families, schools and communities. Psychosocial support i.e. disclosure, support groups should also be encouraged.

Improving adherence to antiretroviral therapy in pediatric patients requires innovative and multifaceted strategies on a sustained basis in order to improve the quality of life of these patients.

### **5.3 Recommendations**

The importance of adherence in this setting needs to be emphasized if the benefits of ART are to be observed. Caregivers in this setting need further education on the importance and benefits of adherence. There is also need for close monitoring of adherence in this setting. Caregivers need to understand the necessity and importance of regular follow ups.

It is important for healthcare givers to consider the primary caregivers' level of education as this will be a key guide in assessing the ability to adhere to the child's medication regimen. Irrespective of the level of education of the caregiver, the importance of intensive education about HIV, ARV medication and relevance of adherence to ART should be underscored before initiation of treatment.

If those who are poverty stricken are to attain optimum adherence, material/financial support should be considered. Such families should be referred to social services/social workers for assistance with accessing resources (financial, housing, transportation and child care). Close adherence monitoring and home based nursing intervention, if sustainable, will help HIV positive children and their poor families to better adhere to prescribed medication regimens.

There is need for a positive social support system that will encourage sharing of responsibility for remembering medication within households if optimum adherence level is to be attained

When the caregiver is seropositive and on ART the health team should pay attention to how he/she takes care of his/her own health as this may mirror how the child's health is taken care of.

ART dosage schedule should be tailored to the daily activities/lifestyle of both the child and the caregiver. Caregivers should also be educated on expected side effects, if adherence is to be achieved.

In order to facilitate adherence comparisons in the different settings, there is need for standardization of procedures to assess adherence/non-adherence, with clear adherence cut off points.

**Further research should be conducted in the following areas:-**

- Effect of primary caregiver economic status on adherence to ART in pediatric patients.
- Effect of primary caregiver gender and age on adherence to ART in pediatric patients.
- The effect of HIV disclosure on Quality of Life of pediatric patients. The results of this study should lead to the formulation of guidelines on disclosure of HIV to the child, therefore facilitate adherence.

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**APPENDICES**

**Appendix I: Interview with the Caregiver**

INTRODUCTION TO INTERVIEW WITH THE CARE-GIVER

This interview is aimed at establishing the degree to which our people use ARV drugs and particularly in children. This will help the relevant authorities to put in place measures that will improve children’s intake of antiretroviral thus ensuring better health for the infected children. It should take 10 minutes to complete. Your identity will not be associated with your responses. You are free to ask questions about the research.

**Confirmation and Consent**

I confirm that I have freely agreed to participate in the pediatric ART adherence research project. I have been briefed on what this involves and I agree to the use of the findings as described above. I understand that the material is protected by a code of professional ethics.

**Participant**

**signature:**

\_\_\_\_\_

Names:

\_\_\_\_\_

Date:

\_\_\_\_\_

I confirm, for the project team, that we agree to keep the undertakings in this contract.

**Researcher’s**

**signature:**

\_\_\_\_\_

Name:

\_\_\_\_\_

Date:

\_\_\_\_\_

**Date of the interview.....**

**Interview code.....**

**A) SOCIO-DEMOGRAPHIC CHARACTERISTICS**

i). Sex of the care-giver (1) Male  (2) Female

ii). Age of care-giver in years:.....

iii) What is the care-givers current marital status?

- 1) Single (no partner)   
 2) Married

iv) How is the caregiver related to the child?

- 1) Parent: mother  father   
 2) Guardian   
 3) Foster care

vi) How many children are under your care?

- NONE   
 1 – 5   
 6 And above

vii) Age of the child

1. 0 – 5 years   
 2. 6 – 12 years

viii) Sex of the child. Male  Female

**B) SOCIO-ECONOMIC INFORMATION.**

i) What is the care-givers source of income?

- 1) Full time formal Employment   
 2) Part time formal Employment   
 3) Self-employed   
 4) Unemployed

ii) What is the care-givers average monthly income?.....KSHS

iii) What is the care-givers level of education?

- 1) No formal education   
 2) Primary level   
 3) Secondary level   
 4) University/college level

**C) PSYCHO-SOCIAL OPINION ON ARV DRUGS.**

I. What ART drugs are the child currently on? Can you identify them?

Yes  No

ii. How long has the child been on ARV?

- 1) 2 months-2years  2) 3-5years  3) Over 5 years

iii) In your opinion what are ARV drugs used for?

- 1) Reducing progression of HIV [ ]
- 2) Curing HIV [ ]
- 3) Reducing pain [ ]
- 4) I don't know. [ ]

iv. What is your opinion on ART therapy? 1) Approve [ ] 2) Disapprove [ ]

If \_\_\_\_\_ disapprove, \_\_\_\_\_ what \_\_\_\_\_ are \_\_\_\_\_ the reasons?.....

.....  
 .....  
 .....

v) If Parent, are you also on ARVs? Yes [ ] No [ ]

vi) If on ARV, do you find it difficult to adhere to your own medication? Yes [ ] No [ ]

vii) Who else is responsible for administering the medication?

- 1-primary care-giver solely.....
- 2-other- specify.....

Viii) Many people find it hard to administer every single dose, in the last 24hrs has the child missed a dose of any of the medication? 1- Yes, 2- No

ix) If yes how many doses have you forgotten to give the child?

**MISSED DOSE(S) REPORT**

Complete Prior to Visit			Complete During Interview	
A	B	C	D	E
Drug Name(s)	Drug Code	Expected No of doses.	Reported No of doses.	Missed Doses in the past 24 hrs
a)				
b)				
c)				
d)				

x. Are you able to follow the child's ARV therapy regimen? Yes [ ] No [ ]

x) In the last one month have you utilized any of the following aids for improving adherence? 1- Yes, 2- No

1- Yes, 2- No, 3-Not known.

- Labels [ ]
- Calendars [ ]
- Pill boxes [ ]
- Beepers [ ]

Monitoring caps  [ ]  
 Diary  [ ]

**xi)** Are there any drug related problems or situations that make it hard to give the child every dose of medication everyday? 1- Yes, 2- No  
 If yes, could you cite at least 3 problems.....  
 .....

Drug related adherence difficulties

	Drug No 1 Name	Drug No 2 Name	Drug No 3 Name	Drug No 4 Name	Drug No 5 Name
Problem Identified 1- yes 2-No	<input type="checkbox"/> [ ]				
Reason for non-adherence					
a)cant get drug	<input type="checkbox"/> [ ]				
b)Didn't refill/ ran out.	<input type="checkbox"/> [ ]				
c) spits out; amount	<input type="checkbox"/> [ ]				
d)side- effects/toxicity	<input type="checkbox"/> [ ]				
e)Scheduling interferes with lifestyle( school, meals, sleep)	<input type="checkbox"/> [ ]				
f)Child refuses	<input type="checkbox"/> [ ]				
g)Multiple caretakers	<input type="checkbox"/> [ ]				
g)Concerns about disclosure.	<input type="checkbox"/> [ ]				
i)Inter-current illness	<input type="checkbox"/> [ ]				
g)Other. Specify					

xii) Is the child currently on any other drug? Yes  [ ] No  [ ]  
 If yes, is it adversely affecting ARV administration? Yes  [ ] No  [ ]

Xiii) If child is over 5 years, is the child aware of his/her disease? Yes  [ ] No  [ ]

Xiv) if not, are you willing to let the child know? Yes  [ ] no  [ ]

Xv) In your opinion, how would this knowledge or lack of it affect drug administration? 1. Adversely 2. Does not affect 3. It encourages.

Xvi) If the child attends school, do the teachers know about his/her status? Yes [ ]  
No [ ]

xvii) Are you willing to let the teacher know? Yes [ ] No [ ]

xviii) What benefits have you seen from the child's use of ARV medication? 1) Weight gain [ ] 2) normal growth [ ] 3) reduced ill-health [ ]

xix) Are you willing to continue administering the medication? Yes [ ] No [ ]

xx) What can be done to help you adhere to ART?

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.....  
.....  
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**THANK YOU FOR YOUR PARTICIPATION**

## Appendix II: Drug Code References Anti – Hiv Drugs

08180407.....	Abacavir /ABC / Ziagen/ 1592U89
08180025.....	Alovudine/CL-184824
08181205.....	Amprenavir/APV/Agenerase/141W94/VX-479
08181214.....	Atazanavir/ATV ?BMS-232632
08180006.....	Azidouridine/AzdU/azido-2'3'-dideoxyuridine
08180018.....	Ateviridine mesylate U-87201E
08180021.....	AZT/ZDV/Zidovudine/Retrovir
08180032.....	CD4/RST4
08180412.....	Combivir(3TC/ZDV)
08180024.....	D4T/Stavudine/Zerit
08180052.....	D4T XR/Zerit XR
08180414.....	DAPD/ Amdoxovir/trimeric
08180020.....	ddC/Zalcitabine/HIVID
08180007.....	ddl/Didanosine/Videx
08180051.....	ddl EC/Didanosine EC/Videx EC
08180031.....	DLV/delavirdine mesylate/Receptop
08180804.....	Efavirenz/EFV/Sustiva/DMP266/Stocrin
08180420.....	Epizocom(Abacavir/lamivudine)
08180411.....	Fluorouridine/935U83
08180415.....	FTC/Emtriva/emtricitabine
08180043.....	Indinavir/IDV/Crixivan
08180013.....	Interleukin-2/IL-2
08181218.....	Lexiva/Fosamprenavir/GW433908
08180026.....	Lamivudine/3TC/Epivir
08181208.....	Lopinavir/Ritonavir(LPV/RTV)/Kaletra/ABT-378/r
08180048.....	Loviride/Lotrene
08181204.....	Nelfinavir/NFV/Viracept
08180013.....	Nevirapine/NVP/Viramune
08181203.....	Ritonavir/RTV/Norvir
08181209.....	Saquinavir soft gel/FTV/Fortovase
08180030.....	Saquinavir/SQ/Invirase/Ro31-8959
08188804.....	T-20/Pentafuside/Enfuvirtide/ENF
08182002.....	TDF/Tenoforir/Tenoforir disoproxil fumerate/Viread
08180418.....	Trizivir(3TC/ABC/ZDV)
08180421.....	Truvada(tenofovir disoproxil(emtricitabine))

### Appendix III: List o ARVs Approved For Treatment of Hiv In Children

Drug class	Approved for paediatric use	Type of formulation				
		capsule	tablet	liquid	powder	Iv
<b>NRTIS</b>						
Abacavir	√		√	√		
<b>Lamivudine</b>	√		√	√		
<b>Zidovudine</b>	√	√	√	√		√
Didanosine	√	√	√		√	
Stavudine	√		√	√		
Emtricitabine	√	√		√		
Zalcitabine	-		√			
Tenofovir DF	-		√			
<b>NNRTIs</b>						
Delaviridine	-	√				
Efavirenz	√	√	√	√		
<b>Nevirapine</b>	√		√	√		
<b>PIs</b>						
Amprenavir	√	√		√		
Lopinavir/ritonavir	√	√	√	√		
Nelfinavir	√		√			
Ritonavir	√	√		√		
Saquinavir	-	√	√			
Fosamprenavir	-		√			
Atazanavir	-	√				
Indinavir	-	√				
Tipranavir	-	√				

**Appendix V: Treatment Regimen**

<b>Regimen</b>	<b>0-3 Years</b>	<b>Over 3 years</b>
First Line	Stavudine(d4T) Lamivudine(3TC) Lapinavir/ritonavir(kaletra)	Stavudine(d4T) Lamivudine(3TC) Efavirenz EFV
Second Line	Zidovudine(AZT) Didanosine(dd) Nevirapine/efavirenz	Zidovudine(AZT) Lopinavir/ritonavir(kaletra) Didanosine(dd)