COMPARATIVE ASSESSMENT ON THE ADHERENCE AND EFFECTIVENESS OF DOLUTEGRAVIR VERSUS LOPINAVIR-BASED REGIMENS AMONG CHILDREN WITH HIV INFECTION IN TANZANIA AND ASSOCIATED FACTORS: A RETROSPECTIVE COHORT STUDY

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By

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A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Pharmacovigilance and Pharmacoepidemiology of

Muhimbili University of Health and Allied Sciences
October, 2024

CERTIFICATION

The undersigned certifies that they have read and recommends for acceptance by Muhimbili University of Health and Allied Sciences of the dissertation entitled; **''Comparative assessment on the adherence and effectiveness of Dolutegravir versus Lopinavir-based regimens among children with HIV infection in Tanzania and associated factors: A retrospective cohort study'',** in (partial) fulfillment of the requirements for the Degree of Master of Pharmacovigilance and Pharmacoepidemiology of Muhimbili University of Health and Allied Sciences.

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Date: _____

DECLARATION AND COPYRIGHT

I, **Deogratius Mussa Panga** declare that this **dissertation** is my original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature..... **Date**.....

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DEDICATION

This work is dedicated to my lovely family for their unwavering support and encouragement throughout this study. Their faith and interest in understanding the use of medicines and their associated adverse events which has now become an integral part of my daily life.

ABSTRACT

Background: Tanzania bears a significant HIV burden, with around 85,000 children living with the virus as of 2021, according to the United Nations Programme on HIV/AIDS (UNAIDS). The global HIV 95-95-95 targets aim for 95% of people with HIV to be diagnosed, 95% of those diagnosed to be on antiretroviral therapy (ART), and 95% of those on ART to achieve viral load suppression by 2030. Tanzania has achieved significant advancements: 60.6% of individuals with HIV are aware of their status, 93.6% of those who know their status are receiving antiretroviral therapy (ART) and 87% of those on ART have attained viral load suppression. Adhering well to ART is crucial for meeting these goals, particularly for pediatric patients who not only needs safe and effective but also medications tailored for children.

Objective: To compare the adherence and effectiveness of a dolutegravir (DTG) tablet 10mg-versus Lopinavir (LPV/r) based regimens among HIV-infected children in Tanzania and associated factors.

Methodology: This retrospective cohort study was conducted from January 2021 to November 2023 at three selected CTC clinics in Tanzania: Muhimbili National Hospital, Mbeya Zonal Referral Hospital, and Baylor College of Medicine Bugando- Mwanza. The study included children who had been on the DTG and Lopinavir-based regimen for at least six months to one year without prior exposure to other HIV treatment regimens. Adherence was measured by assessing the patients' refilling schedule of medicine and effectiveness was assessed by viral load suppression (HVL < 50 copies/ml). Data were collected using a structured case report forms and then analyzed using SPSS version 23. Descriptive statistics summarized the data, and associations between regimens adherence and effectiveness were evaluated using modified poison regression.

Results: The study included 340 participants. Adherence rates were significantly higher among those on the DTG regimen (95.9%) compared to those on the Lopinavir/ritonavir (LPV/r) regimen (85.1%) ($P < 0.001$) 95 % CI. Adverse drug events (ADEs) were significantly lower in the DTG group (8.7%) compared to the LPV/r group (22.0%) ($p < 0.001$). Factors which were

significantly associated with good adherence included being aged ≥ 5 years (aRR = 1.08, p = 0.04) 95 % CI, the presence of an active caregiver (aRR = 1.40, p = 0.006) 95 % CI, and the absence of ADEs (aRR = 1.28, p = 0.008) 95 % CI. Viral load suppression rates were higher in the DTG group at both at 6 and 12 months compared to the LPV/r group.

Conclusion and Recommendation: The DTG regimen is associated with higher adherence and better effectiveness in achieving viral load suppression among pediatric patients compared to the LPV/r regimen. These findings support the use of DTG as a preferred treatment option for children with HIV. Ongoing monitoring and support for caregivers are recommended to enhance adherence and improve treatment outcomes. Further research with longer follow-up periods and diverse populations is needed to confirm these findings and assess long-term outcomes.

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immuno Deficiency Syndrome
ART	Antiretroviral Therapy
ADR-	Adverse Drug Reaction
ADE	Adverse Drug Event
CTC	Care and Treatment Center
DTG 10 mg	Dolutegravir 10 mg
EMLc	Essential Medicines List for Children.
HIV	Human Immuno-deficiency Virus
INSTI	Intergrase Strand Transfer Inhibitor
LPV/r	Lopinavir/ritonavir
MoH	Ministry of Health
MUHAS	Muhimbili University of Health and Allied Sciences
TLD	Tenofovir Lamivudine Dolutegravir
TMDA	Tanzania Medicines and Medical Devices Authority
UNAIDS	United Nations Programme on HIV/AIDS
WHO	World Health Organization
IPTW	Inverse probability treatment weighting.
GEE	Generalized estimating equation.
Prof	Professor

DEFINITIONS OF TERMS

Adherence: Refers to the extent to which a person follows the recommended course of treatment prescribed by their healthcare provider. In this study a refill adherence of ≥ 95% is considered as good adherence and patients with <95 % are considered to have poor adherence.

An adverse drug event: Is an undesirable occurrence that occurs in the context of drug treatment but which may or may not be causally related to a medicine.

Adverse drug reaction: Is an unintended and noxious effect that is attributable to a medicine when it has been given within the normal range of doses used in humans.

Anti-retroviral therapy clinic: Refers to a unit in a hospital that is responsible for counseling, diagnosing and treating HIV infected person using Anti-retroviral viral medications.

Effectiveness: Refers to how well a medication achieves its intended therapeutic effect in real-world clinical settings.

Viral load suppression: Having < 50copies/ml.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

In 2017, about 10% of the 36.9 million people living with HIV were children and adolescents, with approximately 80% of them in Sub-Saharan Africa (1). Despite significant progress in HIV treatment, the burden of HIV/AIDS among children and adolescents remains significant. In 2020, there were an estimated 3.4 million children and adolescents living with HIV globally, with 300,000 new HIV infections and 131,000 AIDS-related deaths in this age group, mainly in the Eastern and Southern African regions (2). Tanzania also faces a significant burden of HIV infection, with around 85,000 children living with HIV by the end of 2021, according to UNAIDS (3).

ART being a corner stone for HIV management, Dolutegravir, a second-generation Intergrase Strand Transfer nhibitor (INSTI), blocks the integration of HIV-1 DNA into the host genome, preventing viral replication. It has demonstrated excellent effectiveness in both newly treated and previously treated adults, leading to high rates of viral suppression and improved immune system outcomes. Due to its effectiveness, tolerability, and low risk of resistance, now DTG has become the preferred first choice for adult ART regimens in many countries (4). Despite having DTG based regimen as the preferred choice there is limited information on adherence and effectiveness in pediatric population in Tanzania.

DTG works by disrupting the activity of the HIV Intergrase-DNA complex, it is quickly absorbed, reaching peak blood concentration a few hours after ingestion, and its half-life of 12 hours allows for once-daily administration without the need for pharmacological enhancement. The drug is primarily metabolized through hepatic glucuronidation by UDP-glucuronosyltransferase, with minimal excretion through urine (5).

Pediatric populations, including HIV-infected children, have unique considerations when it comes to drug safety. Physiological differences, organ maturation and developmental changes which can impact drug metabolism and cause potential adverse events (6).

Advantages of the DTG 10 mg formulation in the pediatric population include improved dosage accuracy (7) allowing for more precise dosing based on children's weight and age, ensuring they receive the appropriate amount of medication. This formulation may also offer a better safety profile compared to other dose formulations, reducing the risk of potential side effects in pediatric patients (8). Despite the lower dosage, the 10 mg formulation of DTG maintains its efficacy in managing HIV infection in children, providing effective treatment outcomes. Additionally, the improved palatability of this formulation may makes it easier for children to adhere to their treatment regimen, while its convenience in terms of administration and storage simplifies the medication management process for caregivers and healthcare providers (7). According to the HIV 95-95-95 worldwide targets, by 2030, 95% of people living with HIV must be diagnosed, 95% of diagnosed must be on antiretroviral therapy (ART), and 95% of those on ART must have viral load suppression. To achieve the final 95 target, adherence to treatment is essential, highlighting the significance of this investigation (9).

This study compares the adherence and effectiveness of the DTG 10mg tablet versus the LPV/r-based regimen among HIV-infected children in Tanzania, as the management approach has shifted from LPV/r to DTG-based regimens.

1.2 Problem statement

The implementation of successful ART in the 1990s significantly decreased AIDS-related deaths and illnesses. Adherence to ART emerged as a crucial factor for long-term survival. Moreover, globally, effective ART which relies on optimal adherence, has also become a key preventive measure against the continued spread of the disease at the population level (1).

ART based on DTG is becoming increasingly popular throughout the world since it is very effective and well-tolerated in adults (10). In most trials evaluating DTG, the percentage of children and adolescents with viral suppression at 12 months of age was high (>70%) and ranged from 42% to 83% (11).

Despite progress in reducing new HIV infections in children, and AIDS-related deaths and illnesses, Africa is still behind in reaching the 95-95- 95 fast-track global targets for ending AIDS among children by 2030 (9).

Regardless of of the safety and efficacy of DTG in treating HIV, still there is limited information regarding its effectiveness and adherence specifically in Tanzanian pediatric population (12,13).

There is a scarcity of studies showing or comparing the effectiveness and adherence of past HIV treatment with current treatment. Tanzania is the country where adherence among young populations living with HIV has not been broadly investigated particularly on DTG the new treatment. Martell et al. conducted a study to assess adherence in a pediatric population in rural Tanzania in Tanzania.(1) However, this study did not take into account the new treatment and effectiveness of that treatment. This study focus to address this knowledge gap by evaluating the effectiveness and adherence of DTG tablet 10 mg based regimen in comparison with the previous treatment (LPV/r)

1.3 Conceptual frame work

Figure 1 describes the relationship on how effectiveness of DTG 10 mg based regimen can be influenced or changed by different factors. Good adherence to DTG 10 mg eventually uplifts the effectiveness of the treatment. However, several factors also influence adherence as shown in the conceptual framework. Younger children may struggle with adherence due to factors such as dependence on caregivers for medication administration. Sex-related pharmacokinetic and pharmacodynamics variations could affect the drug's effectiveness in male and female pediatric patients. Weight can play a significant role in medication adherence and effectiveness, especially in pediatric patients. As weight fluctuates the caretaker of the child may fail to adhere to medication especially in case of weight losses. Dosage calculations are often weight-dependent, and under or overestimating the dose based on weight can affect adherence. For example, in case of weight gain number of tablets may increase when dose changes to 20mg or 30mg increased number of tablets can lead to poor adherence. Monitoring weight changes and adjusting dosages should be done with counselling.

Adherence, which is a key factor in determining the effectiveness of treatment, is influenced by various clinical factors. These include the presence of reported adverse drug events, availability of medications, and previous experience with regimen changes, age, sex, presence of active care giver at home. If an individual has reported an adverse drug reaction, faced issues with the availability of treatment, or has had to change their treatment regimen in the past, these factors can affect the overall adherence and effectiveness of the therapy.

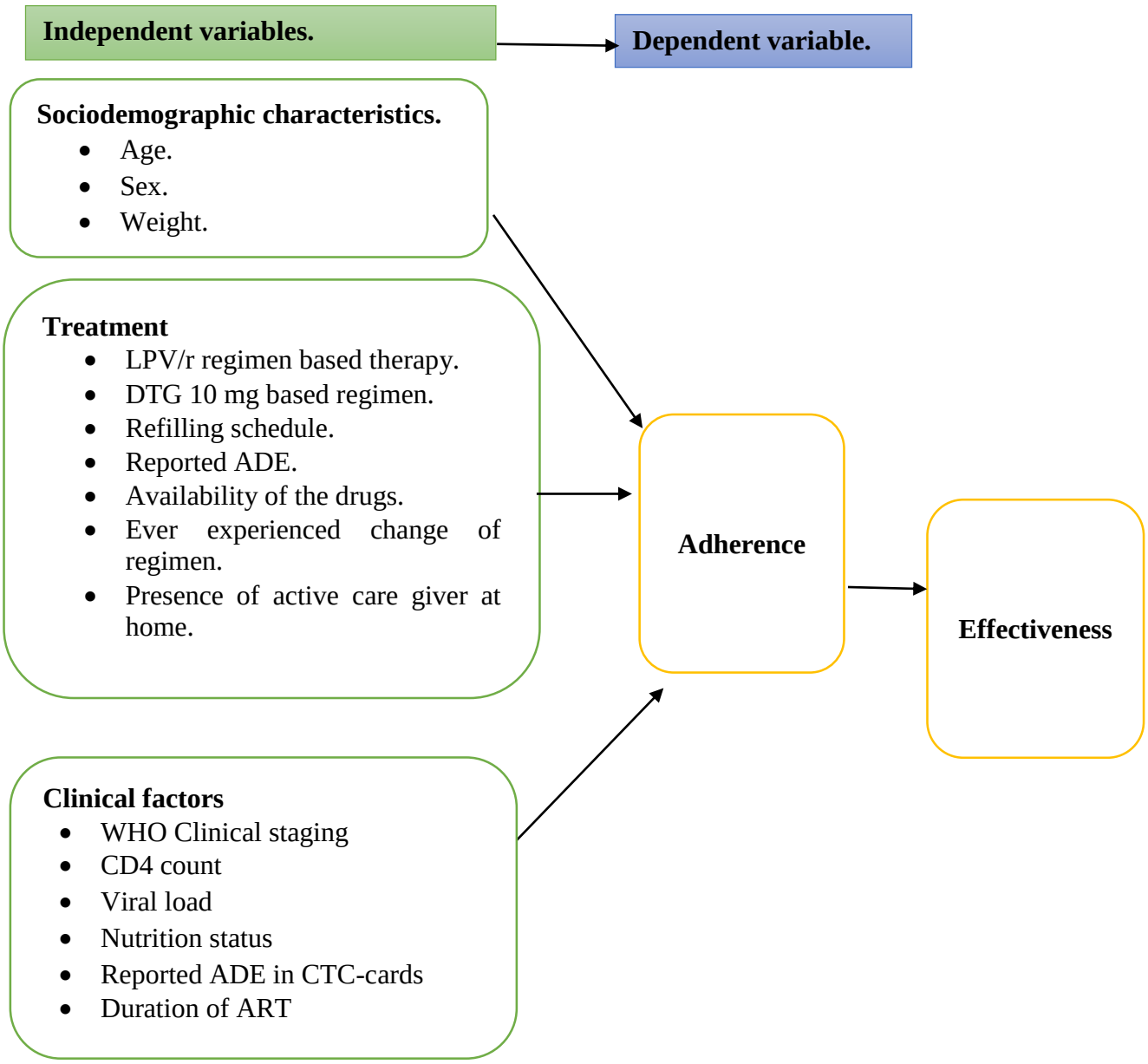


Figure 1: Conceptual framework to show the relationship between the outcome and independent variables.

1.4 Rationale

The results of this study offers more valuable knowledge to healthcare providers and policymakers, assisting them in making well-informed decisions about the use of DTG based regimen in pediatric patients and enhancing the overall management of HIV infection in children. Policy makers can use this information to update treatment guidelines and recommendations for pediatric HIV management. In addition, knowledge of the adherence rate and effectiveness can help policy makers allocate resources effectively.

1.5 Research questions

1.5.1 Main research question

What is the level of adherence and effectiveness of DTG 10 mg versus LPV/r based regimens among HIV infected children in Tanzania?

1.5.2 Sub Research questions

1. What is the adherence level of DTG 10 mg versus LPV/r based regimen among HIV-infected children in Tanzania?
2. What factors influence adherence to DTG 10 mg and LPV/r based regimen among HIV-infected children in Tanzania?
3. What is the effectiveness of DTG 10 mg versus LPV/r based regimen among HIV-infected children in Tanzania?
4. What factors impact the effectiveness of DTG 10 mg and LPV/r based regimen among HIV-infected children in Tanzania?

1.6 Study hypothesis

Null hypothesis (H0): There is no significant difference in adherence and effectiveness between the DTG 10 mg based regimen and the LPV/r based regimen among HIV-infected children in Tanzania.

Alternative hypothesis (H1): There is a significant difference in adherence and effectiveness between the DTG 10 mg based regimen and the LPV/r based regimen among HIV-infected children in Tanzania.

1.7 Objectives

1.7.1 Main Objective

To compare the level of adherence and effectiveness of DTG 10 mg versus LPV/r based regimen among HIV infected children in Tanzania.

1.7.2 Specific Objective

1) To compare the adherence level of DTG 10 mg versus LPV/r based regimen among HIV-infected children in Tanzania.
2) To investigate factors influencing adherence to the DTG 10 mg and LPV/r based regimen among HIV-infected children in Tanzania.
3) To assess effectiveness of the DTG 10 mg versus LPV/r based regimen for HIV-infected children in Tanzania.
4) To assess factors influencing effectiveness of the DTG 10 mg and LPV/r based regimen among HIV-infected children in Tanzania.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Adherence of dolutegravir

Ensuring that patients take their medications as prescribed by their healthcare providers is crucial for achieving the full health benefits of a specific medication-based treatment. Patients, particularly those with chronic illnesses, often encounter challenges in following a recommended treatment regimen, leading to non-adherence (NA) to medications. This non-adherence affects a significant percentage of patients, with average rates of around 30-50%, presenting a significant obstacle (12,13).

Non-adherence to medications is a major challenge in the real-life treatment of chronically ill patients. To meet this challenge, adherence interventions with a tailored approach towards patient-specific adherence barriers is necessary (14).

The Intergrase transfer inhibitor DTG has recently replaced the non-nucleoside reverse transcriptase inhibitors (efavirenz and nevirapine) in several Sub-Saharan African countries, including Tanzania. Since this change, there is limited data on the current treatment outcomes focusing on treatment-experienced HIV-infected patients switched to DTG based regimens in pediatric as well as in adult in Tanzania (15).

ART must be taken daily over one's lifetime to maintain viral suppression in individuals living with human immunodeficiency virus (HIV).The current clinical practice the emphasis has been placed on maintaining an ART adherence threshold of 95 % or greater to maintain virology suppression and to prevent the development of drug resistance. However the 95% threshold is based on findings from several studies and has been extrapolated to all ART regimens including dolutegravir based regimen(16).

2.2 Factors that may affect the adherence

The negative effects caused by ART, known as adverse drug reactions (ADRs), are a leading reason for alterations in medications, low adherence, resistance, and treatment ineffectiveness.

It is essential to assess the frequency of ADEs in pediatric patients undergoing ART. In a research study carried out in Ethiopia, the medical records of 186 pediatric patients receiving ART were examined, and it was found that of the 153 patients who were reviewed, a total of 23 (15%) ADR were observed (17).

Allergic reactions have been documented and were identified by the presence of a rash, general symptoms, and occasionally organ dysfunction, such as liver damage. These occurrences were reported in less than 1% of individuals who received DTG 50mg tablets in Phase 3 clinical trials in which discontinuation of DTG 50mg tablets or DTG Dispersible tablets 10 mg and any suspected agents was done immediately. This as a result led to non-adherence (18).

A study conducted in Africa to understand and improve viral load suppression in children, observed that, drug availability is critical for adherence. Drug stock outs or supply disruptions was shown to compromise treatment outcomes. In addition, it was reported that, patients who have experienced changes in their regimen faced challenges with adherence due to regimen complexity, side effects, or psychological factors related to treatment changes. Understanding the reasons for regimen changes and addressing any barriers to adherence is important for optimizing treatment outcomes (9).

A study conducted in Tanzania to check for adherence to ART among children and adolescents, showed that socio demographic factors are outlined to affect the adherence and effectiveness of ART treatments in pediatric population including age, sex and weight. It was also shown that, younger children may struggle with adherence due to factors such as dependence on caregivers for medication administration, understanding of treatment importance, or challenges with the medication's taste or form. Older children may exhibit better adherence due to increased independence and understanding of their condition (1).

A study conducted in Nigeria in 2013 to assess factors influencing adherence to pediatric antiretroviral therapy, reported that, longer duration on ART may influence adherence behavior, with some patients experiencing adherence fatigue over time. Monitoring adherence over the course of treatment is important for optimizing treatment outcomes (19).

2.3 Factors that may affect effectiveness

A study conducted in Tanzania in 2019 reported that, children under the age of five and especially male participants were more inclined to achieve viral suppression in comparison to others, although this difference was not statistically significant. The study also showed age-related differences in drug metabolism and absorption could affect the effectiveness of DTG 10 mg. Younger children may require dosage adjustments based on age-specific pharmacokinetic considerations to achieve optimal effectiveness (1).

A study conducted in Africa in 2021 described that, nutrition status assessment plays a role in overall health and immune function, which can influence the effectiveness of DTG 10 mg in managing HIV infection. Support on optimal nutrition can lead better treatment outcomes. The study also showed that, sex-related pharmacokinetic and pharmacodynamics variations could affect the drug's effectiveness in male and female pediatric patients. Understanding these differences is essential for optimizing treatment outcomes (9).

Furthermore, a study by Judd et al. looking at factors associated with non-adherence to ART, indicated that young age was the main predictor for non-adherence to medications which leads to low effectiveness of the treatment (20).

Moreover, the duration of ART has been reported to impact treatment outcomes, including the effectiveness of DTG 10 mg. This was reported by a study by Berihun et al 2023. The study showed long-term adherence is essential for sustained viral suppression and optimal health outcomes (21).

Weight-related differences in drug distribution and metabolism has been reported to influence the effectiveness of DTG 10 mg. Proper dosing based on weight considerations is crucial to ensure the drug reaches therapeutic levels for optimal effectiveness in pediatric patients. Considering these variables such as age, sex, and weight when assessing adherence and effectiveness of DTG 10 mg in pediatric patients with HIV infection is essential for tailored treatment approaches, dosage adjustments, and monitoring strategies to achieve improved outcomes in this vulnerable population (10).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

The study design was retrospective cohort study. Cohort one were children from 3 kg up to 19 kg whom their first ever treatment was DTG 10 mg based regimen and cohort two were children who were in LPV/r based regimen before the introduction of DTG 10 mg based regimen. This design was chosen as it would be useful in determining the effectiveness of DTG 10 mg based regimen.

3.2 Study setting

The study was conducted at 3 CTC clinics including Muhimbili National Hospital, Baylor Clinic in Mbeya Zonal Referral Hospital and Baylor Clinic in Mwanza Region.

Mbeya Zonal Referral Hospital is the HIV Care and Treatment Clinic that was operated by Baylor college of Medicine Children's Foundation in Mbeya region in Southern Tanzania and currently operated by the government. Baylor is a patient-centered, pediatrics HIV prevention and treatment program providing direct care to more than 6224 children.

Baylor College of Medicine in Bugando Medical Center is located in Mwanza region. This is the HIV Care and Treatment Clinic that is operated by Baylor college of Medicine Children's Foundation in Mwanza region in Tanzania providing direct care to more than 5000 children.

Muhimbili National Hospital is the largest referral hospital in Tanzania, located in Dar es Salaam. It is a major teaching hospital that provides a wide range of medical services and specialized care. Also the hospital has the HIV children's clinic, which focuses on providing care and treatment specifically for children affected by HIV/AIDS. This clinic plays a vital role in managing HIV in children, offering support, treatment, and education to improve their health outcomes.

3.3 Study population

The study recruited HIV sero-converted children with weight of 3 kg to 19 kg on DTG regimen based therapy and children who were on LPV/r regimen based therapy before the introduction of DTG 10 mg based regimen.

Exposed.

These were children who have never been in previous treatment, only new treatment (DTG regimen based therapy from July 2022 up to November 2023).

Unexposed

Unexposed population does not consider receiving DTG-based regimen, will only be considered for previous treatment (LPV/r regimen based therapy before the introduction of DTG 10 mg based regimen) from January 2021 to June 2022.

3.4 Study duration

Data collection commenced in April 2024 and continued through May 2024.

3.5 Estimation on the sample size

The following formula was used for sample size calculation is for cohort study design.

$$n = \frac{\{Z_\beta \sqrt{[P1\,(1-P1) + P0\,(1-P0)]} + Z_\alpha \sqrt{[2\,\bar{p}\,(1-\bar{p})]}\}^2}{(P0-P1)^2}$$

Where,

n= Sample size for each group

P1= the proportion of viral load suppression among children with weight of 3kg to 19 kg on dolutegravir regimen (exposed)

P0=the proportion of viral load suppression among children who were in Lopinavir regimen based therapy before the introduction of dolutegravir 10 mg based regimen (Unexposed)

$\bar{p}$ =The average proportion exposed

Average proportion exposed ($\bar{p}$) = (P1+ P0)/2

Z_β= 0.84 for power (1-β) of study is 80%

Z_α= Desired level of statistical significance, for 0.05 significance level= 1.96

(Z_α= the standard normal deviate at 95 confidence level=1.96 for two-sided comparisons depending on the hypothesis being tested).

Thus, assuming that,

Z_β= for 80% power is 0.84,

Z_α= for 0.05 significance level= 1.96

- p_1 = 0.79 (proportion of viral load suppression among children on dolutegravir regimen according to Bacha et al (2)
- p_1 P_0= 0.63 (proportion of viral load suppression among children who were in Lopinavir regimen based therapy before the introduction of dolutegravir 10 mg based regimen according to Antonucci et al (1)

$$p_1 \quad n = \frac{\{0.84\sqrt{[0.79(1-0.79) + 0.62(1-0.62)]} + 1.96\sqrt{[2 \times 0.705 (1-0.705)]}\}^2}{0.02}$$

Sample size (n) = 90.

Accounting for a design effect of 1.5= 135

Taking into account a 10% allowance for incomplete data, the sample size consisted of 150 patients. A total of 300 patients was calculated, including 150 children on DTG regimen and 150 children who were previously on a LPV/r based therapy before the introduction of the DTG 10 mg regimen.

3.6 Eligibility criteria

Eligibility criteria for exposed

1. HIV sero-converted children with body weight of 3 kg to 19 kg on DTG regimen based therapy and who were never in previous HIV treatment based regimen (LPV/r).
2. Children who have been on DTG regimen for a minimum of six to twelve months.

Eligibility criteria for non-exposed

1. Children who were in LPV/r regimen based therapy for at least for six to twelve months.

Exclusion criteria for exposed

1) Terminally ill children, those with chronic comorbidities and those on long-term medications
2) Those with missing clinical records and incomplete medical records from database.

3.7 Data collection methods

Data were collected from the patients' files and from the system that was available at the specific facility attending the CTC clinic such as CTC 2. A total of 340 patients' data were collected while during sample size calculation the minimum sample size was 300, this shows that during data collection more data were captured so as to increase the power of study and case report form was used for data collection.

3.8 Study variables

Dependent variables

Assessment of adherence

Adherence to DTG 10 mg was assessed using the documented pharmacy refill schedule whereby the calculation of refill adherence percentage was calculated by the following formula (22);

$$\% = \frac{(\text{number of days for the pills dispensed previously} - \text{delay in days for next pick up})}{\text{Number of days of pills dispensed previously}} * 100$$

The pharmacy refill record was collected at each pharmacy visitation to collect medication depending on their respective schedule, overall percentage adherence was be obtained by calculating the average percentage from all the records visits. Based on HIV treatment guideline patient with refill adherence $\geq$ 95 were considered to have good adherence and < 95% poor adherence (23,24)(3).

Assessment of effectiveness

To assess effectiveness of DTG 10, 6-months, and 12-months HVL records were collected.
The cutoff for effectiveness (suppressed) was VL< 50 copies /ml while for not effective (not suppressed) was VL $\geq$ 50 copies /ml.

Independent variables.

Independent variables included age, level of support from family, nature and severity of the disease, CD4, sex, dates such as of HIV diagnosis, of ART initiation, side effects of the medication, type of regimen (DTG 10 mg / LPV/r), and duration on the regimen.

3.9 Sampling procedures

Simple random sampling was used as sampling technique in this study. The selection of the CTC clinics which were Mbeya Zonal Referral Hospital and Baylor Clinic was done because these were the main two dedicated pediatric clinics that focus on HIV infected children in Tanzania with of almost 6000 and 5000 clients, respectively. Muhimbili National Hospital this is the only national referral facility in the country and also has the CTC clinic that serves both adults and pediatric in integrated manner.

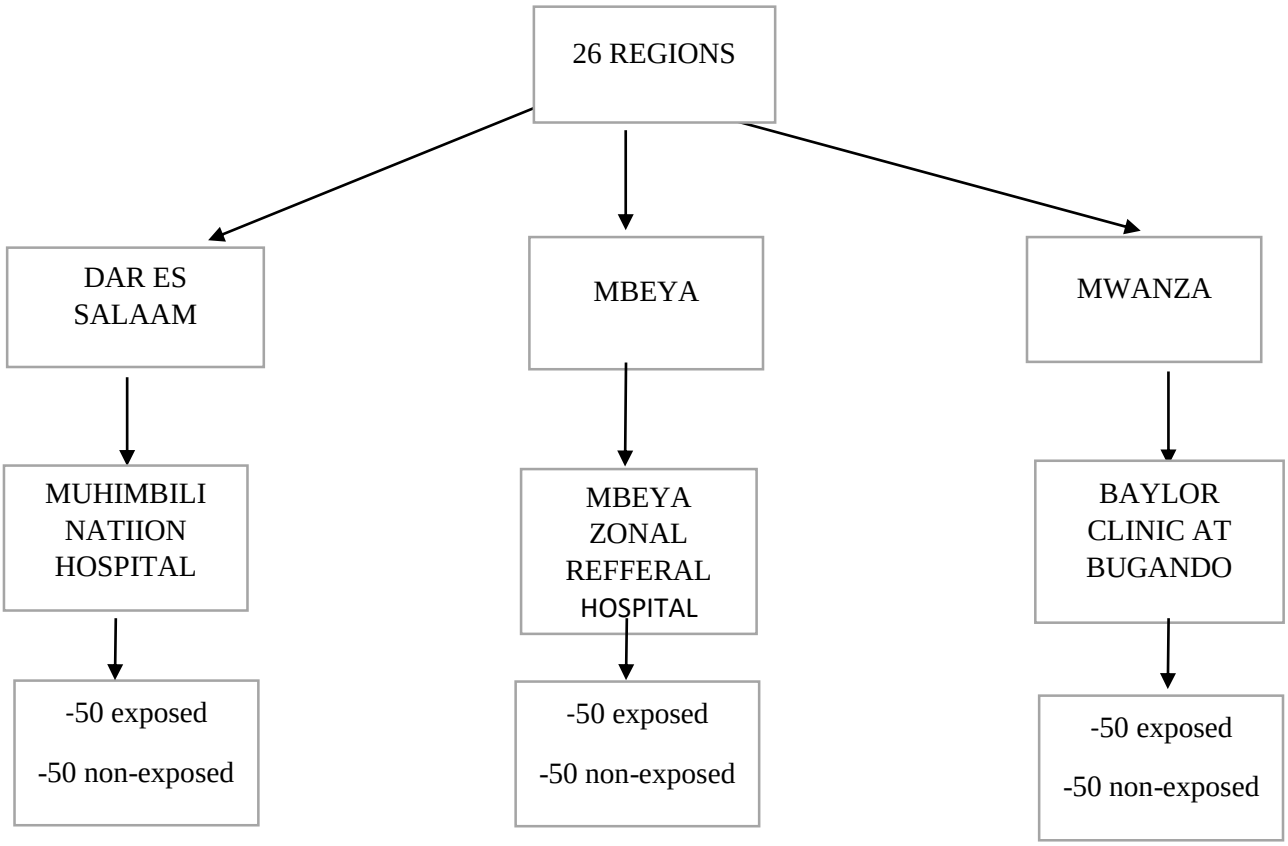


Figure 2: Shows how sampling of study cites was done.

Patient history information

The data collection tool (***appendix 1***) collected comprehensive clinical information on the files to guide the exclusion process and to provide a quantitative answer to the study objectives as follows:

Clinical examination

Some variables were collected following clinical examination, including anthropometric measurements.

Bodyweight was measured in Kilogram (Kg) using a calibrated weighing scale to the nearby 0.5 Kg.

Laboratory investigations

The following variables were collected from patents whose laboratory samples have been performed:

- Viral load, both at 6 and at 12 months.
- CD_4 count at baseline, 6 and 12 months.

3.9.1 Pre testing of the tools

Pretesting of the tools was done with 10% of the sample size at Mwananyamala Hospital. A sample of 30 patients who meet the study's eligibility criteria who were similar to the target study population in terms of demographics characteristics, management and medical history, were selected for the pretesting. This population was not be included in the main study.

3.9.2 Data analysis

IBM SPSS version 23 was used for data analysis. Descriptive statistics was conducted to obtain summaries of variables. Numerical variables such as age and CD4 counts were summarized using median (IQR) and frequency for categorical variable. Modified poison regression was used to compare the (dependent outcome) which was viral load suppression and the Independent variable (ART type) of the two cohorts (DTG and LPV/r) regimen based therapy. Proportion of patients with viral suppression was presented in percentages. Generalized Estimating Equations (GEE) are a statistical method used for analyzing correlated data, particularly in longitudinal studies or clustered data.

Inverse Probability of Treatment Weighting (IPTW) was done to create a balance between the two groups by using the baseline demographic and clinical characteristics of the study participants making them more comparable and balanced.

Associations of factors between adherence and effectiveness of the two regimens were assessed using Modified poison regression. Variables with a p value < 0.2 were included in the multivariate analysis. In multivariate analysis, logistic regression was conducted to identify an independent effect of each variable to either adherence or effectiveness of DTG 10 mg regimen based therapy. While 95% CI and p values <0.05 were considered statistically significant**.**

3.10 Ethical considerations

The study commenced after receiving approval from the Muhimbili University of Health and Allied Sciences (MUHAS-IRB). The reference number for the approval was MUHAS-REC-04-2024-2129 (Appendix 2). Further approval to conduct the study was requested and granted from the Executive Directors of the respective institutions. Consent forms were not applied in this study because data and information were collected from the patients file and electronic system available at the place of study site. To ensure confidentiality, documents were stored in secured places which was only be accessible to the researcher. Special coding was used instead of names of patients and information during the study.

3.11 Dissemination plan

The findings of this study will be disseminated through multiple channels to ensure broad reach and impact. Firstly, a comprehensive report was prepared and submitted to the dean School of Pharmacy, head of department Clinical Pharmacy and Pharmacology at Muhimbili University of Health and Allied Sciences (MUHAS).

In addition to internal dissemination, the results will be shared at national and international conferences focusing on HIV treatment and pediatric care to reach a wider professional audience. Efforts will be made to publish the study in peer-reviewed journals, thereby contributing to the global body of knowledge and allowing other researchers and practitioners to access and apply the insights gained.

CHAPTER FOUR

4.0 RESULTS

4.1 Baseline socio-demographic and clinical characteristics of the study participants.

Baseline socio-demographic and clinical characteristics of study participants on two different ART regimens, DTG and LPV/r. A higher percentage of participants on DTG were from Baylor Mwanza (37.8%) compared to those on LPV/r (21.4%), with a statistically significant p-value of 0.003. Conversely, Mbeya Zonal had a higher proportion of participants on LPV/r (48.8%) compared to those on DTG (35.5%). The MNH facility had similar distributions for both groups, with 26.7% on DTG and 29.8% on LPV/r.

Age group analysis revealed a significant difference, with 50.9% of participants on DTG being under 5 years old, compared to 70.2% on LPV/r ($p < 0.001$). For participants aged 5 years and above, the proportions were 49.1% on DTG and 29.8% on LPV/r.

In terms of sex distribution, there was no significant difference between the two groups. Males constituted 48.8% of the DTG group and 43.5% of the LPV/r group ($p = 0.319$), while females made up 51.2% of the DTG group and 56.5% of the LPV/r group.

The presence of an active caregiver was slightly higher in the DTG group (91.3%) compared to the LPV/r group (86.3%), but this difference was not statistically significant ($p = 0.146$). Similarly, prior exposure to ART showed no significant difference, with 18.6% of DTG participants and 14.3% of LPV/r participants having prior exposure ($p = 0.283$).

The patient category on diagnosis indicated that a higher proportion of participants in the DTG group were in the early presentation category (77.9%) compared to the LPV/r group (70.8%), though this difference was not significant ($p = 0.083$). The late presentation category and late with advanced disease had comparable distributions between the groups.

Examining the WHO clinical stage of participants, there were no significant differences across stages. Stage I had 30.2% of DTG participants and 23.2% of LPV/r participants ($p = 0.158$). Stages II, III, and IV also showed similar distributions without significant differences.

However, the reported adverse drug events (ADE) showed a significant difference, with 8.7% of participants on DTG reporting ADEs compared to 22.0% on LPV/r ($p < 0.001$). This indicates a higher incidence of ADEs among participants on LPV/r.

In terms of age in months, the median age for the DTG group was significantly lower at 45 months (IQR 26-62) compared to 57 months (IQR 49-65) for the LPV/r group ($p < 0.001$). Median baseline CD4 counts and median percentile Body mass for age Z score (BAZ) which was calculated using the WHO anthroplus did not show significant differences between the groups. The median baseline CD4 count for the DTG group was 655 (IQR 474-873) compared to 584 (IQR 450-950) for the LPV/r group ($p = 0.358$). Similarly, the median percentile BAZ was 0.25 (IQR 0.02-0.69) for the DTG group and 0.20 (IQR 0.01-0.67) for the LPV/r group ($p = 0.408$).Table 1 showing baseline characteristics of study participants.

Table 1: Baseline socio-demographic and clinical characteristics of the study participants. (N=340)

Variable	DTG n = 172, n (%)	LPV/r n = 168, n (%)
Health facility		
Baylor Mwanza	65 (37.8)	36 (21.4)
Mbeya Zonal	61 (35.5)	82 (48.8)
MNH	46 (26.7)	50 (29.8)
Age group (years)		
< 5	87 (50.9)	118 (70.2)
≥ 5	84 (49.1)	50 (29.8)
Sex		
Male	84 (48.8)	73 (43.5)
Female	88 (51.2)	95 (56.5)
Active caregiver		
Yes	157 (91.3)	145 (86.3)
No	15 (8.7)	23 (13.7)
Prior exposure to PMTCT		
Yes	32 (18.6)	24 (14.3)
No	140 (81.4)	144 (85.7)
Category on diagnosed		
Early presentation	134 (77.9)	119 (70.8)
Late presentation	34 (19.8)	37 (22.0)
Late with advanced	4 (2.3)	12 (7.1)
WHO stage		
Stage I	52 (30.2)	39 (23.2)
Stage II	78 (45.3)	71 (42.3)
Stage III	35 (20.3)	45 (26.8)
Stage IV	7 (4.1)	13 (7.7)
Reported ADE		
Yes	15 (8.7)	37 (22.0)
No	157 (91.3)	131 (78.0)
Median age in months (IQR)	45 (26, 62)	57 (49, 65)
Median Baseline CD4 (IQR)	655 (474, 873)	584 (450, 950)
Median Percentile BAZ (IQR)	0.25 (0.02, 0.69)	0.20 (0.01, 0.67)

ART regimens and adherence

ART regimen and adherence demonstrates a clear difference in adherence rates between participants on DTG and those on LPV/r based regimens. Specifically, the proportion of participants with good adherence to ART was significantly higher among those on the DTG regimen (95.9%, 95% CI 91.8% - 98.0%) compared to those on the LPV/r regimen (85.1%, 95% CI 79.0% - 89.7%) and the $p < 0.001$. This indicates that participants on the DTG regimen were more likely to adhere well to their treatment compared to those on the LPV/r regimen. The confidence intervals for both regimens indicate a high level of precision in the estimates, with non-overlapping intervals suggesting a statistically significant difference in adherence rates between the two regimens. Figure 3 showing the association between ART regimens and adherence.

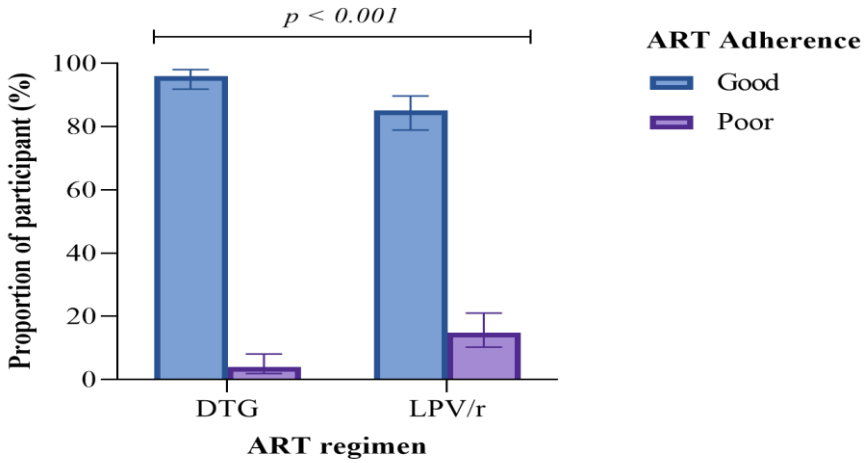


Figure 3: The association between ART regimen and adherence among patients on DTG based regimen compared to those on LPV/r based regimen.

4.2 Univariable and multivariable analysis of the factors associated with good adherence

Univariable and multivariable analysis of the factors associated with good adherence. Participants from Baylor Mwanza exhibited a high adherence rate of 92.1%, with a crude relative risk (cRR) of 1.07, although this was not statistically significant (p=0.206). Similarly, participants from Mbeya Zonal also showed a high adherence rate of 92.3% with a cRR of 1.07,

which was not statistically significant (p=0.164). In this context, Muhimbili National Hospital (MNH) served as the reference group.

Age emerged as a significant factor, with participants aged ≥ 5 years demonstrating a notably higher adherence rate of 95.5%, reflected by a cRR of 1.09 (p=0.006). This indicates that older children were more likely to adhere well to ART. Conversely, younger participants (< 5 years) served as the reference group. When examining sex, female participants had a good adherence rate of 91.8% with a cRR of 1.03, though this was not statistically significant (p=0.413), with males serving as the reference group.

The presence of an active caregiver significantly increased adherence, with 94.0% of participants with an active caregiver adhering well, resulting in a cRR of 1.49 (p=0.001). Those without an active caregiver served as the reference group. Prior exposure to ART did not show a significant association with adherence, with a cRR of 1.01 (p=0.890) for those with prior exposure, compared to the reference group of participants without prior exposure.

Presentation at diagnosis also influenced adherence, as early presenters category had a higher adherence rate of 94.9%, with a cRR of 1.27, although this was not statistically significant (p=0.105). Late presenters served as the reference group. When considering WHO clinical stage, participants in Stage I had the highest adherence rate of 97.8%, with a cRR of 1.30 (p=0.041), whereas stages II, III, and IV did not show significant associations with adherence.

Reported adverse drug events (ADEs) had a marked impact on adherence. Participants without ADEs had significantly higher adherence at 94.4%, with a cRR of 1.36 (p<0.001), compared to those with ADEs who served as the reference group.

Moving to the multivariable analysis, adjustments for potential confounders were made to identify independent predictors of good adherence. The health facility remained an area of interest; however, after adjustment, the association was not significant for Baylor Mwanza (aRR = 0.97, p=0.521) or Mbeya Zonal (aRR = 0.93, p=0.208), with MNH continuing as the reference group.

Age continued to be a significant predictor, as participants aged ≥ 5 years maintained a higher adherence rate with an adjusted relative risk (aRR) of 1.08 (p=0.040), compared to those aged < 5 years. The presence of an active caregiver remained a robust predictor of good adherence, with an aRR of 1.40 (p=0.006), highlighting the critical role of caregiver support.

In terms of WHO clinical stage, the initial significance observed in univariable analysis for Stage I did not hold in the multivariable analysis (aRR=1.15, p=0.346), and stages II, III, and IV showed no significant association with adherence. The absence of reported ADEs remained significantly associated with good adherence, with an aRR of 1.28 (p=0.008), reinforcing the importance of managing side effects to maintain adherence.

In summary, the analysis identifies age (≥ 5 years), the presence of an active caregiver, and the absence of ADEs as significant factors associated with good adherence. While factors like health facility and WHO stage appeared significant in the univariable analysis, only a few retained significance after adjusting for confounders in the multivariable analysis. This indicates the robustness of the results, underscoring the key determinants of adherence to ART.As shown in table 2.

Table 2: Univariable and multivariable analysis of the factors associated with good adherence

			Good. Adherence	Univariable analysis			Multivariable analysis		
Variable	**Category**	**Total**	**n (%)**	**cRR**	**95% CI**	**p-value**	**aRR**	**95% CI**	**p - value**
Health facility	Baylor Mwanza	101	93 (92.1)	1.07	0.97 – 1.17	0.206	0.97	0.87 – 1.08	0.521
	Mbeya Zonal	143	132 (92.3)	1.07	0.97 – 1.17	0.164	0.93	0.84 – 1.04	0.208
	MNH	96	83 (86.5)	Ref					
Age (years)	≥ 5	134	128 (95.5)	1.09	1.03 – 1.17	0.006	1.08	1.01 – 1.16	**0.040**
	< 5	205	179 (87.3)	Ref					
Sex	Female	183	168 (91.8)	1.03	0.96 – 1.10	0.413			
	Male	157	140 (89.2)	Ref					
Active caregiver	Yes	302	284 (94.0)	1.49	1.17 – 1.90	0.001	1.40	1.10 – 1.78	**0.006**
	No	38	24 (63.2)	Ref					
Prior exposure to PMTCT	Yes	56	51 (91.1)	1.01	0.92 – 1.10	0.890			
	No	284	257 (90.5)	Ref					
Presentation at diagnosis	Early	253	240 (94.9)	1.27	0.95 – 1.68	0.105			
	Late	71	56 (78.9)	1.05	0.77 – 1.43	0.748			
	advanced	16	12 (75.0)	Ref					
WHO stage	Stage I	91	89 (97.8)	1.30	1.01 – 1.68	0.041	1.15	0.92 – 1.44	0.346
	Stage II	149	137 (91.9)	1.23	0.95 – 1.59	0.121	1.11	0.89 – 1.39	0.346
	Stage III	80	67 (83.8)	1.12	0.85 – 1.46	0.425	1.09	0.86 – 1.38	0.478
	Stage IV	20	15 (75.0)	Ref					
Reported ADE	No	288	272 (94.4)	1.36	1.14 – 1.64	< 0.001	1.28	1.07 – 1.53	**0.008**
	Yes	52	36 (69.2)	Ref					

Key: cRR: crude Relative Risk, aRR: adjusted Relative Risk, Ref: Reference, G. Adh: good adherence

4.3 Assessment of effectiveness of the ART based regimens for HIV-infected children in Tanzania

The socio-demographic characteristics of the study participants before and after IPTW were analyzed before and after applying IPTW to adjust for potential confounding factors. Initially, a significant difference was observed in the distribution of participants across the three health

facilities. Baylor Mwanza had a higher proportion of participants on the DTG regimen (37.8%) compared to those on the LPV/r regimen (21.4%), while Mbeya Zonal had more participants on the LPV/r regimen (48.8%) compared to the DTG regimen (35.5%). Muhimbili National Hospital (MNH) showed a relatively balanced distribution between the two regimens. These differences were statistically significant (p=0.003). However, after IPTW adjustment, the distribution across health facilities became more balanced and no longer statistically significant (p=0.948).

Age group differences were notable before weighting, with a higher proportion of younger children (<5 years) on the LPV/r regimen (70.2%) compared to the DTG regimen (50.9%), resulting in a statistically significant difference (p<0.001). After IPTW adjustment, the age distribution between the two regimens balanced out, with no significant difference (p=0.932). Similarly, the sex distribution was initially not significantly different, with females slightly more represented in the LPV/r group (56.5%) compared to the DTG group (51.2%). This balance remained after weighting, with no significant changes (p=0.590).

The presence of an active caregiver was slightly higher in the DTG group before weighting (91.3%) compared to the LPV/r group (86.3%), but this difference was not statistically significant (p=0.146). After IPTW, the proportions remained similar and statistically non-significant (p=0.931). Prior exposure to ART was also not significantly different between the groups before (p=0.283) and after weighting (p=0.714), with a slightly higher percentage in the DTG group.

Regarding the category of diagnosis, before weighting, a higher proportion of early presenters were on the DTG regimen (77.9%) compared to the LPV/r regimen (70.8%), although this was not statistically significant (p=0.083). After IPTW adjustment, the proportions were closely matched and non-significant (p=0.859). WHO staging also showed no significant differences before and after weighting, with stages I, II, III, and IV distributed similarly between the two regimens.

Reported adverse drug events (ADEs) were significantly higher in the LPV/r group (22.0%) compared to the DTG group (8.7%) before weighting ($p<0.001$). After IPTW, the difference in reported ADEs remained but was less pronounced and statistically non-significant ($p=0.710$).

The adherence rates among participants on the DTG regimen were significantly higher compared to those on the LPV/r regimen. Specifically, before applying IPTW, 95.9% of participants on DTG exhibited good adherence compared to 85.1% on LPV/r ($p < 0.001$), indicating a significant difference favoring DTG. After IPTW adjustment, the adherence rates remained high for both groups, with 92.6% of DTG participants and 89.8% of LPV/r participants showing good adherence, though the difference was no longer statistically significant ($p = 0.366$). This analysis highlights that DTG is associated with better adherence rates compared to LPV/r, even after adjusting for confounding factors. (Table 3 showing the difference before and after IPTW)

Table 3: Socio-demographic and clinical characteristics of the study participants, before and after IPTW

Variable	Before IPTW			After IPTW		
	DTG (%)	LPV (%)	p - value	DTG (%)	LPV (%)	p - value
Health facility						
Baylor Mwanza	65 (37.8)	36 (21.4)	**0.003**	59 (36.4)	58 (34.7)	0.948
Mbeya Zonal	61 (35.5)	82 (48.8)		60 (37.0)	64 (38.3)	
MNH	46 (26.7)	50 (29.8)		43 (26.5)	45 (26.9)	
Age group (years)						
< 5	87 (50.9)	118 (70.2)	< **0.001**	90 (55.6)	93 (56.0)	0.932
≥ 5	84 (49.1)	50 (29.8)		72 (44.4)	73 (44.0)	
Sex						
Male	84 (48.8)	73 (43.5)	0.319	78 (48.1)	75 (45.2)	0.590
Female	88 (51.2)	95 (56.5)		84 (51.9)	91 (54.8)	
Active caregiver						
Yes	157 (91.3)	145 (86.3)	0.146	140 (86.4)	144 (86.7)	0.931
No	15 (8.7)	23 (13.7)		22 (13.6)	22 (13.3)	
Prior exposure to PMTCT						
Yes	32 (18.6)	24 (14.3)	0.283	30 (18.4)	28 (16.9)	0.714
No	140 (81.4)	144 (85.7)		133 (81.6)	138 (83.1)	
Category diagnosed						
Early presentation	134 (77.9)	119 (70.8)	0.083	124 (76.5)	125 (75.3)	0.859
Late presentation	34 (19.8)	37 (22.0)		33 (20.4)	34 (20.5)	
Late with advanced disease	4 (2.3)	12 (7.1)		5 (3.1)	7 (4.2)	
WHO stage						
Stage I	52 (30.2)	39 (23.2)	0.158	41 (25.2)	36 (21.6)	0.873
Stage II	78 (45.3)	71 (42.3)		77 (47.2)	81 (48.5)	
Stage III	35 (20.3)	45 (26.8)		36 (22.1)	41 (24.6)	
Stage IV	7 (4.1)	13 (7.7)		9 (5.5)	9 (5.4)	
Reported ADE						
Yes	15 (8.7)	37 (22.0)	< **0.001**	23 (14.2)	26 (15.7)	0.710
No	157 (91.3)	131 (78.0)		139 (85.8)	140 (84.3)	
Adherence						
Good	165 (95.9)	143 (85.1)	< **0.001**	150 (92.6)	149 (89.8)	0.366
Poor	7 (4.1)	25 (14.9)		12 (7.4)	17 (10.2)	

Socio-demographic and clinical characteristics of the study participants, before and after IPTW continuous variable

Variable	Before IPTW			After IPTW		
	DTG	LPV/r	p - value	DTG	LPV/r	p - value
Median Baseline CD4 (IQR)	655 (474, 873)	584 (450, 950)	0.358	644 (450, 854)	560 (450, 788)	0.386
Median Percentile BAZ (IQR)	0.25 (0.02, 0.69)	0.20 (0.01, 0.67)	0.408	0.29 (0.02, 0.73)	0.15 (0.00, 0.6)	0.111

The baseline characteristics of the study participants, before and after the application of inverse probability of treatment weighting (IPTW), provide insight into the comparability of the two groups on dolutegravir (DTG) and Lopinavir/ritonavir (LPV/r) regimens. Initially, the median baseline CD4 count for participants on the DTG regimen was 655 cells/mm³ (IQR: 474-873) compared to 584 cells/mm³ (IQR: 450-950) for those on the LPV/r regimen. This difference was not statistically significant (p=0.358). After IPTW adjustment, the median baseline CD4 count for the DTG group slightly decreased to 644 cells/mm³ (IQR: 450-854), and for the LPV/r group, it decreased to 560 cells/mm³ (IQR: 450-788). The p-value remained non-significant (p=0.386), indicating that the CD4 counts were balanced across the groups after weighting.

The median percentile Body Mass Index-for-age Z-score (BAZ) was initially 0.25 (IQR: 0.02-0.69) for the DTG group and 0.20 (IQR: 0.01-0.67) for the LPV/r group, with no significant difference (p=0.408). After IPTW adjustment, the median percentile BAZ for the DTG group increased to 0.29 (IQR: 0.02-0.73) while it decreased for the LPV/r group to 0.15 (IQR: 0.00-0.6). Despite these changes, the difference between the groups remained non-significant (p=0.111), suggesting that the nutritional status of the participants was comparable after adjustment. The non-significant p-values both before and after IPTW indicate that the differences in these baseline characteristics were not substantial, ensuring a more reliable assessment of treatment outcomes.

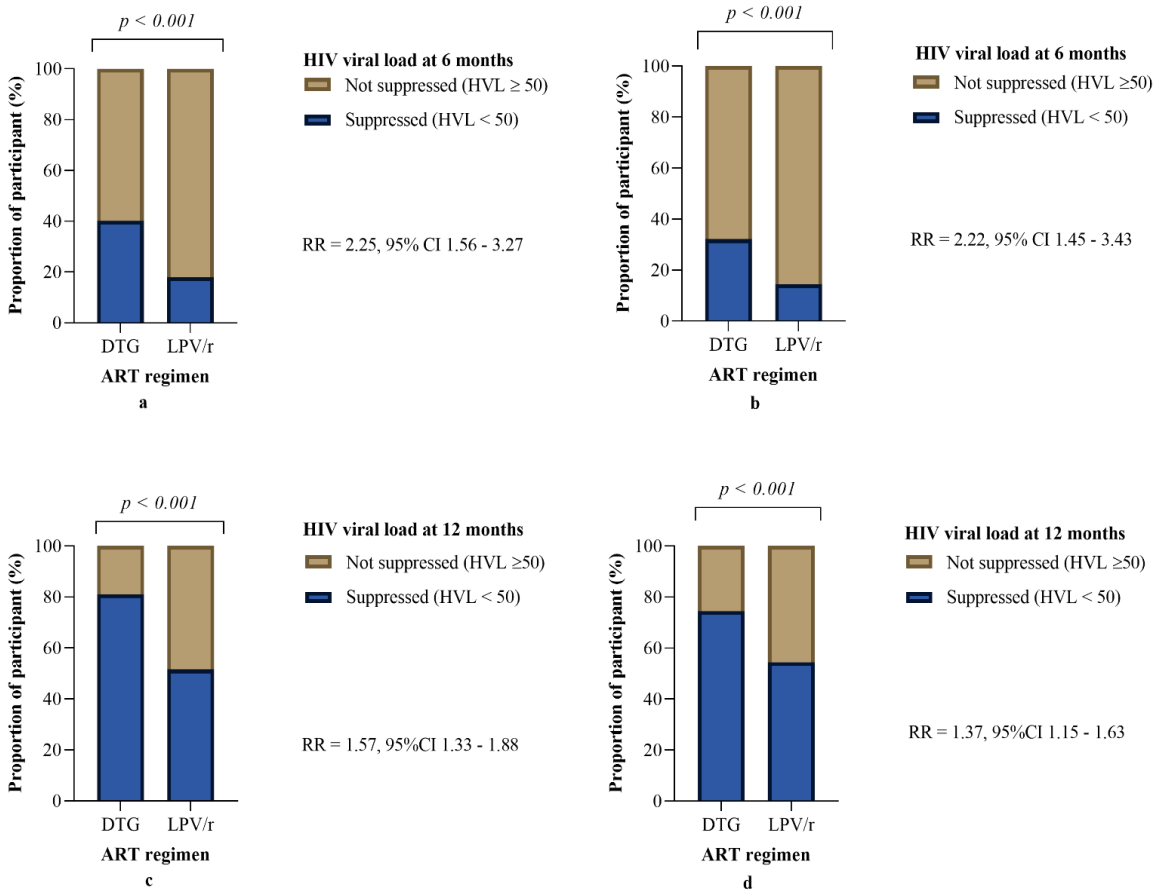


Figure 4: Association between ART regimen and effectiveness at 6 and 12 months, both before and after the application of (IPTW).

The association between ART regimen and effectiveness, the proportion of participants with HIV suppression to ART at 6 months before weighting at after weighting i.e. **a** and **b** respectively while for effectiveness at 12 months before and after weighting as presented in points **c** and **d** respectively.

4.4 Univariable and multivariable analysis of the factors associated with HIV viral load suppression at 6 and 12 months (GEE).

Health facility: Neither the Baylor Mwanza nor Mbeya Zonal facilities showed a significant association with viral load suppression compared to the reference facility (MNH).

Age was another important factor. For participants aged ≥ 5 years, the univariable analysis showed no significant association (cRR 1.03, 95% CI 0.87-1.22, p = 0.737). This was consistent in the multivariable analysis where age still showed no significant association (aRR 1.03, 95% CI 0.87-1.22, p = 0.737). Sex: Being female was not significantly associated with viral load suppression in either the univariable or multivariable analyses.

The presence of an active caregiver was a significant factor in the univariable analysis (cRR 2.20, 95% CI 1.44-3.37, p < 0.001). However, in the multivariable analysis, the association was no longer significant (aRR 1.35, 95% CI 0.91-1.99, p = 0.140.

The presentation category, particularly early presentation, was significantly associated with viral load suppression in the univariable analysis (cRR 4.03, 95% CI 1.62-10.02, p = 0.003). In the multivariable analysis, this association remained significant (aRR 2.83, 95% CI 1.16-6.91, p = 0.023).

WHO stage was another factor analyzed. In the univariable analysis, Stage I was significantly associated with viral load suppression (cRR 2.22, 95% CI 1.21-4.07, p = 0.010). However, this significance did not hold in the multivariable analysis (aRR 1.18, 95% CI 0.67-2.07, p = 0.569).

Adverse drug events: Reported adverse drug events showed a significant association with higher viral load suppression in the univariable analysis, but not in the multivariable analysis.

Adherence to ART was a strong predictor of viral load suppression. In the univariable analysis, good adherence was significantly associated with suppression (cRR 4.24, 95% CI 1.78-10.11, p = 0.001). This strong association remained significant in the multivariable analysis (aRR 2.86, 95% CI 1.23-6.68, p = 0.015).

In summary, the key factors that remained significantly associated with higher viral load suppression in the multivariable analysis were early presentation of HIV and good adherence to ART. These findings highlight the importance of timely diagnosis and consistent adherence in achieving viral load suppression among people living with HIV. (As shown in table 4)

Table 4: Univariable and multivariable analysis of the factors associated with HIV viral load suppression at 6 and 12 months (GEE)

		Univariable analysis			Multivariable analysis		
Variable	**Category**	**cRR**	**95% CI**	**p-value**	**aRR**	**95% CI**	**p-value**
Health facility	Baylor Mwanza	0.92	0.74 – 1.15	0.473			
	Mbeya Zonal	0.93	0.76 – 1.14	0.484			
	MNH	Ref					
Age (years)	≥ 5	1.03	0.87 – 1.22	0.737			
	< 5	Ref					
Sex	Female	1.04	0.87 – 1.23	0.679			
	Male	Ref					
Active caregiver	Yes	2.20	1.44 – 3.37	< 0.001	1.35	0.91 – 1.99	0.140
	No	Ref					
BAZ		1.01	0.98 – 1.05	0.461			
PMTCT Prior exposure	Yes	1.00	0.90 – 1.12	0.948			
	No	Ref					
Presentation	Early	4.03	1.62 – 10.02	0.003	2.83	1.16 – 6.91	**0.023**
	Late	1.97	0.76 – 5.09	0.161	1.76	0.71 – 4.33	0.220
	Late with advanced	Ref					
WHO stage	Stage I	2.22	1.21 – 4.07	0.010	1.18	0.67 – 2.07	0.569
	Stage II	1.86	1.02 – 3.40	0.043	1.06	0.61 – 1.84	0.832
	Stage III	1.19	0.63 – 2.27	0.595	0.98	0.56 – 1.70	0.933
	Stage IV	Ref					
Reported ADE	No	1.65	1.18 – 2.32	0.004	1.14	0.86 – 1.50	0.374
	Yes	Ref					
Adherence	Good	4.24	1.78 – 10.11	0.001	2.86	1.23 – 6.68	**0.015**
	Poor	Ref					

Key: cRR: crude Relative Risk, aRR: adjusted Relative Risk, Ref: Reference, HVL Supp: HIV viral load suppression

CHAPTER FIVE

5.0 DISCUSSION

This study evaluated the adherence and effectiveness of the DTG regimen compared to the LPV/r regimen among children with HIV in Tanzania. The findings provide significant insights that could influence clinical practices and healthcare policies. The baseline socio-demographic and clinical characteristics of the participants revealed distinct differences between those on DTG and LPV/r regimens. Participants on DTG were more likely to be from Baylor Mwanza (37.8%) compared to those on LPV/r (21.4%). Age also played a critical role, with a higher proportion of younger children (<5 years) on the LPV/r regimen (70.2%) compared to DTG (50.9%).

The study found significantly higher adherence rates among participants on the DTG regimen (95.9%) compared to those on LPV/r (85.1%). The substantial difference in adherence rates may be attributed to DTG's better tolerability and fewer side effects, making it easier for children and healthcare supporters to follow their medication regimen. The high adherence rate in the DTG group supports the potential benefits of this regimen in managing pediatric HIV. These results were in line with the results from Kilapilo et al (24) which reported adherence of 78% and the study conducted by Mutagonda et al which reported adherence of 71% (22).

Adverse drug events were more commonly reported among participants on the LPV/r regimen (22.0%) compared to those on DTG (8.7%). This significant difference underscores the better safety profile of DTG, which can positively impact adherence. The lower incidence of ADEs in the DTG group suggests that this regimen might be more suitable for children, reducing the likelihood of treatment discontinuation due to adverse effects. Similar findings were also reported by Kilapilo ,Mutagonda et al (2,22,24) very few individuals reported to encounter ADE.

Regardless the DTG-based regimen has reduced ADE reports as compared to other regimen WHO still recommend a follow-up and monitoring (25).

The effectiveness of the ART regimens was evaluated based on HIV viral load suppression rates at 6 and 12 months. Before applying inverse probability of treatment weighting (IPTW), the DTG regimen showed higher effectiveness at both time points compared to LPV/r. At 6 months, the effectiveness of DTG was 40.1%, whereas LPV/r was 17.8%. After IPTW adjustment, these rates were 32% for DTG and 14.5% for LPV/r. Similarly, at 12 months, DTG had an effectiveness rate of 81% compared to 51.2% for LPV/r, with adjusted rates of 76% and 54%, respectively. The findings from this study are consistent with the results reported in other relevant studies. Specifically, previous research conducted by Maganda, Moore CL and Kilapilo et al (10,15,24) has also shown high rates of viral load suppression among children receiving DTG-based antiretroviral therapy. In these studies, the reported viral suppression rates for DTG-based regimens were 89% and 87%, respectively. The findings from national survey in Tanzania that was conducted by Kamori et al had similar results on the overall viral load suppression in children of 74.4 % (26).

Further analysis identified key factors influencing adherence and viral load suppression. The presence of an active caregiver was significantly associated with good adherence (aRR 1.40, p = 0.006), emphasizing the importance of caregiver support in managing pediatric HIV treatment. These results were similar to other studies done by Kilapilo et al (24) where the presence of healthcare supporters increases adherence. Additionally, older children (≥ 5 years) showed higher adherence rates (aRR 1.08, P= 0.040) in contrast to children < 5, similar results were presented by (27).

The absence of ADEs reports also significantly predicted good adherence. For viral load suppression, early presentation at diagnosis and good adherence were significant factors, highlighting the necessity of timely diagnosis and consistent treatment adherence. The study revealed significant differences in adherence rates and viral load suppression between the two regimens, highlighting the superior performance of DTG in the pediatric population. These findings align with and expand upon previous research, emphasizing the critical role of medication tolerability and caregiver support in achieving optimal treatment outcomes.

Adherence to ART is crucial for its effectiveness. The study found significantly higher adherence rates among participants on the DTG regimen (95.9%) compared to those on LPV/r (85.1%). This is consistent with previous research which highlighted that better tolerability and fewer side effects associated with DTG contribute to higher adherence rates. For instance, a study by Bacha (2) demonstrated that DTG-based regimens led to significant improvements in adherence among children in Eastern and Southern Africa, emphasizing the drug's potential to achieve better treatment outcomes.

The effectiveness of the ART regimens was evaluated based on HIV viral load suppression rates at 6 and 12 month. In line with our findings, Antonucci et al (1) observed higher viral load suppression rates with DTG compared to other regimens among children and adolescents in Tanzania. Our results showed that at 12 month, the DTG regimen had an effectiveness rate of 81% compared to 51.2% for LPV/r, further supporting the superior performance of DTG in achieving viral suppression. This aligns with a previous study by Walmseley which reported that DTG to have a higher efficacy due to its robust pharmacological profile and better tolerability (5).

The study also identified key factors influencing adherence and viral load suppression, such as the presence of an active caregiver and early diagnosis. This was in line with a study done by Penazzato et al which found that caregiver support significantly enhanced adherence among children on ART, leading to improved treatment outcomes (28). Moreover, other studies by UNICEF (9) and (29) highlighted that early diagnosis and initiation of treatment are crucial for achieving optimal viral suppression, which is reflected in our findings where early presentation at diagnosis was associated with better adherence and effectiveness.

ADEs were more commonly reported among participants on the LPV/r regimen (22.0%) compared to those on DTG (8.7%). This significant difference underscores the better safety profile of DTG, which can positively impact adherence. The lower incidence of ADEs in the DTG group is consistent with findings from a previous study by Walmsley which reported fewer side effects among patients on DTG, contributing to its higher adherence rates and overall effectiveness (5).

These findings contribute new insights into the pediatric HIV treatment landscape by demonstrating that the DTG regimen not only improves adherence rates but also significantly enhances viral load suppression compared to the LPV/r regimen. While previous studies by Bacha, Walmsley et al have highlighted the effectiveness and tolerability of DTG. Additionally, these findings emphasize the critical roles of caregiver support and early diagnosis, reinforcing the importance of holistic approaches in managing pediatric HIV. This study fills a significant gap in localized data, offering evidence-based recommendations that could influence treatment guidelines and improve health outcomes for children with HIV in similar settings.

CHAPTER SIX

6.0 LIMITATIONS, CONCLUSIONS, AND RECOMMENDATIONS

6.1 Study limitations and mitigations

This study acknowledges several limitations that could impact the findings and their generalizability. One primary limitation was the reliance on secondary data, which might be incomplete or missing crucial information. To mitigate this, we employed thorough data verification processes, cross-referencing patient files with electronic records to ensure accuracy and completeness.

Another limitation was the potential for improper documentation of data related to patient adherence, as it is dependent on accurate record-keeping by healthcare providers and caregivers. To address this, we used multiple sources of data, such as pharmacy refill records and clinical notes, to triangulate and validate the adherence information.

Additionally, the study was conducted in selected tertiary health facilities, which may not fully represent all settings in Tanzania. While this limits the generalizability of the findings, we have provided detailed descriptions of the study context and population to help others assess the applicability of the results to different settings.

Lastly, the dynamic nature of HIV treatment guidelines and practices could influence the relevance of the study's findings over time. To address this, the study included the most current treatment protocols and highlighted the need for ongoing research to keep pace with evolving standards of care.

6.2 Conclusions

In conclusion, this study demonstrates that the DTG regimen is associated with higher adherence and better effectiveness in achieving viral load suppression among children living with HIV in Tanzania compared to the LPV/r regimen. The findings highlight the potential benefits of DTG based regimen in pediatric HIV treatment, suggesting that it to be a favorable option due to its better tolerability and fewer reports on adverse drug events. The presence of an active caregiver

and early diagnosis significantly contribute to better adherence and treatment outcomes, emphasizing the importance of caregiver support and timely intervention in managing pediatric HIV.

6.3 Recommendations

- Healthcare providers should keep considering the DTG regimen as a preferred option for pediatric HIV treatment due to its higher adherence rates and effectiveness.
- Strategies to support and educate caregivers should be implemented to enhance adherence among children.
- Further research with a longer follow-up period and inclusion of diverse populations is needed to confirm these findings and assess long-term outcomes. Additionally, prospective studies should be conducted to better control for potential confounding factors and provide more robust evidence on the comparative effectiveness of ART regimens in pediatric populations.

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APPENDICES

Appendix I: Data collection tool

Title: ASSESSMENT OF THE ADHERENCE AND EFFECTIVENESS OF DOLUTEGRAVIR TABLET BASED REGIMEN AMONG CHILDREN WITH HIV INFECTION IN TANZANIA: A RETROSPECTIVE COHORT STUDY.

CASE REPORT FORM.

SECTION A. PATIENT PARTICULARS.

1. Name of the health facility
    a) MNH
    b) MZRH
    c) Baylor-Mwanza

2. Patient ID number
3. Age(month)
4. Sex (M or F)
5. Date diagnosed (dd/mm/yyyy)
6. Date ART started (dd/mm/yyyy)
7. Type of ART regimen
    a) Dolutegravir 10mg based regimen
    b) Lopinavir Based regimen

8. Patient on ART for a duration of (6-12) months
    a) 6 months
    b) 12 months
    c) Others (specify in numbers e.g. 7,8,9,10,11)

9. Patient had prior ARV exposure as PMTCT prophylaxis?

a) Yes
b) No

10. If yes

a) High risk prophylaxis
b) Low risk prophylaxis

11. Patient category on diagnosed

a) Early presentation
b) Late presentation
c) Late presentation with advanced disease (CD 4<200)

SECTION B. CLINICAL INFORMATION/ CHARACTERISTICS

SN	**Parameter**	**Base line**	**6 months**	**12 months**
12	Weight (kg)	**12a.**	**12b.**	**12c.**
13	Height.(cm)	**13a.**	**13b.**	**13c.**

SECTION C. LABORATORY PARAMETERS

SN	**Parameter**	**Base line**	**6 months**	**12 months**
14	Creatinine	**14a.**	**14b.**	**14c.**
15	Hemoglobin	**15a.**	**15b.**	**15c.**
16	ASAT	**16a.**	**16b.**	**16c.**
17	Viral load		**17b.**	**17c.**
18	CD 4	**18a.**	**18b.**	**18c.**
19	WHO clinical staging(use numbers)	**19a.**	**19b.**	**19c.**

SECTION D. ASSESSMENT OF ADHERENCE

20. Reported on ADE

a) Yes
b) No

21. If yes (please tick where appropriate)

a) Skin rashes
b) Anemia
c) Vomiting
d) Diarrhea
e) Nausea
f) Renal dysfunction
g) Hepatitis
h) Fever
i) Abnormal weight gain

22. Type of ADE

a) Serious
b) Non serious

23. Patient failed to proceed with medication due to ADE

a) Yes
b) No

Availability of the drug at the specified facility

24. Ever experienced out of stock of Lopinavir based regimen

a) Yes
b) No

25. If yes for how many days (use numbers)

26. Ever experienced out of stock of Dolutegravir based regimen

    a) Yes
    b) No

27. If yes for how many days (use numbers)

28. Presence of Active caregiver support at home

    a) Yes
    b) No

29. Nutrition status of the patient
    a) Non-malnourished
    b) Moderately malnourished
    c) Severely malnourished
    d) Obese

30. Patient experienced change of regimen
    a) Yes
    b) No

31. If yes in the above question, what was the reason for changing the regimen?
    a) Presence of ADE
    b) Clinical failure
    c) Immunological failure
    d) Virologic failure
    e) Out of stock

32. ART adherence status
    a) Good
    b) Poor

33. If poor in the above question, give the reason

a) Toxicity
b) Share with others
c) Felt better/ improved
d) Too ill
e) Stigma
f) Lack of disclosure
g) Poor infrastructure
h) Cultural factor
i) Economic factor
j) Belief factor
k) Social factor
l) Others (specify)

34. Total number of clinic visits (use numbers)

Eg 6,7,8,9,10,11,12

35. ADHERENCE REFILING %

First visit	**Second visit**	**Third visit**	**Fourth visit**	**Fifth visit**	**Sixth visit**	**Seventh visit**	**Eighth visit**	**Ninth visit**
Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A	Number of days dispensed at specific visit =A
Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B	Number of days delayed /missed from scheduled visit =B
Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C	Total number of days for next visit=C
%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$	%= $\frac{A-B}{C}$

Appendix II: Approval for ethical clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/2129 Date: 02/04/2024

MUHAS-REC-04-2024-2129
DEOGRATIUS MUSSA
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: ASSESSMENT OF THE ADHERENCE AND EFFECTIVENESS OF DOLUTEGRAVIR TABLET 10 MG BASED REGIMEN AMONG CHILDREN WITH HIV INFECTION IN TANZANIA: A RETROSPECTIVE COHORT STUDY.

Reference is made to the above heading,

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 02/04/2024
EXPIRATION DATE OF APPROVAL: 02/04/2025

STUDY DESCRIPTION:
Purpose:
The purpose of this retrospective cohort study is to assess the level of adherence and effectiveness of dolutegravir 10 mg based regimen among HIV infected children in Tanzania.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014554.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain Data Transfer Agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain Material Transfer Agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Apply for and obtain permission to publish the results from National Institute for Medical Research. The application should be before submitting to a publisher and not concurrently through the email publications@nimr.or.tz.
9. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahva Salim Masoud.

Chairperson, MUHAS Research and Ethics Committee

Appendix III: Introduction Letter

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.416/2022

28th March, 2024

The Executive Director,
Muhimbili National Hospital,
P.O. Box 65000,
DAR ES SALAAM.

RE: INTRODUCTION LETTER OF DEOGRATIUS MUSSA

We would like to inform you that the carrier of this letter is Deogratius Mussa with registration number HD/MUH/T.416/2022 a student in the College of Medicine in the School of Medicine at Muhimbili University of Health and Allied Science (MUHAS), pursuing MSc. Pharmacovigilance and Pharmacoepidemiology.

As part of his studies, he will be doing an elective research titled **"Assessment of the Adherence and Effectiveness of Dolutegravir Tablet 10 MG Based Regimen Among Children with HIV Infection in Tanzania: A Retrospective Cohort Study".** he is being supervised by Prof. Appolinary Kamuhabwa from MUHAS and Dr. Solob Ngasa from MNH

The ethical clearance for doing the said research has been given by the University.

Kindly request your assistance and cooperation to our student.

Yours Sincerely,

Mr. Sebe Mohamed
For: DIRECTOR, POSTGRADUATE STUDIES

cc: Deogratius Mussa

9 United Nations Road, Upanga West, P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6, Ext. 1015, Direct Line:+255-22-2151378,Telefax:+255-22-2150465,E-mail:dpgs@muhas.ac.tz,Web:https://www.muhas.ac.tz

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.416/2022

05th April, 2024

The Director General,
Bugando Medical Centre,
P.O. Box 1370,
MWANZA

Re: INTRODUCTION LETTER OF DEOGRATIUS MUSSA

The bearer of this letter is Deogratius Mussa (HD/MUH/T.416/2022), a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MSc. Pharmacovigilance and Pharmacoepidemiology.

As part of his studies he intends to do a study titled: **"Assessment of the Adherence and Effectiveness of Dolutegravir Tablet 10 MG Based Regimen Among Children with HIV Infection in Tanzania: A Retrospective Cohort Study."**

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.

Mr. Sebe Mohamed
For: DIRECTOR, POSTGRADUATE STUDIES

c.c. Deogratius Mussa

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam; Tel. G/Line: +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150455;E-mail:dpgs@muhas.ac.tz;Web:https://www.muhas.ac.tz

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.416/2022

05th April, 2024

The Executive Director,
Mbeya Zonal Referral Hospital,
P.O. Box 419,
MBEYA

Re: INTRODUCTION LETTER OF DEOGRATIUS MUSSA

The bearer of this letter is Deogratius Mussa (HD/MUH/T.416/2022), a student at Muhimbili University of Health and Allied Sciences (MUHAS) pursuing MSc. Pharmacovigilance and Pharmacoepidemiology.

As part of his studies he intends to do a study titled: **"Assessment of the Adherence and Effectiveness of Dolutegravir Tablet 10 MG Based Regimen Among Children with HIV Infection in Tanzania: A Retrospective Cohort Study."**

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.

Mr. Sebe Mohamed
For: DIRECTOR, POSTGRADUATE STUDIES

c.c. Deogratius Mussa

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web:https://www.muhas.ac.tz

Appendix IV: Permission letter

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.: MNH/CRTCU/Perm/2024/165 Date: 05th April, 2024

Head of Department,
Paediatrics and Child Health Dr. Evance Kindly assist, as proposed. 12.04.2024
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH

Name Student	**Deogratius Mussa**
Title	**"Assessment of the Adherence and Effectiveness of Dolutegravir Tablet 10 MG Based Regimen Among Children with HIV Infection in Tanzania: A Retrospective Cohort Study".**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Pof. Appolinary Kamuhabwa (MUHAS)
Co – supervisor	Dr. Solob Ngassa (MNH)
Period	08th April, 2024 to 30th June, 2024

Approval has been granted to the above principal investigators to collect data at MNH. Dissemination of study findings at MNH shall be overseen by **Dr. Solob Ngassa** (MNH) supervisor.

Kindly ensure the named principal investigator abide to the ethical principles and other conditions of the research approval.

Sincerely,

Pallangyo

Dr. Charles K. Pallangyo
For: Head of Clinical research, Training and Consultancy Unit

c.c DMS,
c.c Dr. Solob Ngassa
c.c **Deogratius Mussa**

Upanga West, Kalenga Street, Plot No. 10480/3, P.O. BOX 65000, Dar es Salaam, Tanzania.
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BUGANDO MEDICAL CENTRE

Consultant and Teaching Hospital

Department of: **ADMINISTRATION**

Our Ref: **AB.286/317/01/186**

Date: **29.04.2024**

P.O. Box 1370
Mwanza, Tanzania
Telephones
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Email:hospbugando@gmail.com

Mr. Sebe Mohamed
MUHAS
P.O. BOX 65001
DAR ES SALAAM.

RE: PERMISSION TO COLECT DATA AND INTRODUCTION OF DEOGRATIUS MUSSA AT BUGANDO MEDICAL CENTRE

Reference made to the above subject and your letter dated on 05th April, 2024 with Ref. No. HD/MUH/T. 416/2022.

With this letter is to inform your esteemed office that permission has been granted to collect data titled **"Assessment of the Adherence and Effectiveness of Dolutegravir Tablet 10 MG Based Regimen Among Children with HIV Infection in Tanzania: A Retrospective Cohort Study." at Bugando Medical center in Mwanza Tanzania."**

Thanks,

Lucas Mwihechi
For; DIRECTOR GENERAL

Copy to; Head of Department – **Bugando Medical Centre**

For: DIRECTOR GENERAL
BUGANDO MEDICAL CENTRE
P.O. Box 1370
MWANZA

THE UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

Telegram "Referral Hospital"
Fax No: +255 2503577
Tel: +255 2503456/2503351
Email: info@ mzrh.go.tz

Mbeya Zonal Referral Hospital,
Hospital Hill Road,
P. O. Box 419,
Mbeya.

Please quote:

Ref No: SZEC-2439/ R.A/ 24/04 **08 May 2024**

Deogratius Mussa
REG HD/MUH/T.416/2022
Muhimbili University of Allied Sciences
P.O. Box 2410,
MBEYA.
TANZANIA

Dear Sir,

RE: Request for ethical clearance for Protocol "Assessment of adherence and effectiveness of dolutegravir tablet based regimen among HIV infected children in Tanzania. A retrospective cohort study).

Reference is made to the subject as mentioned earlier.

2. I would like to inform you that the Mbeya Medical Research and Ethics Review Committee received and reviewed the abovementioned protocol. The committee has granted Ethical Clearance approval to carry out the mentioned protocol study activities for one year, from **08 May 2024** to **07 May 2025.**

3. This Ethics Clearance approval bears the following specifications:
   i. That you comply with approved study protocol procedures, and at all times you are responsible for the ethical conduct of your research;
   ii. You must notify the Mbeya Medical Research and Ethics Committee in writing regarding any alteration or deviation to the protocol;
   iii. That you submit progress reports to the Committee every six months;
   iv. If the research has been completed, abandoned, discontinued, or not completed for any reason you are required to submit a final report to the Committee;
   v. Permission to publish the results is obtained from the National Institute for Medical Research
   vi. The approval is given for one year from **08 May 2024 to 07 May 2025;** and,
   vii. If you are unable to complete your research within the one-year validation period you will be required to write to Mbeya Medical Research and Ethics Committee to request an extension; and,
   viii. You must immediately notify the Mbeya Medical Research and Ethics Committee of any adverse event and/or unforeseen events that might affect the continued ethical acceptability of the research.

4. You may contact the undersigned should any additional information be required.

Sincerely,

Executive Director
Mbeya Zonal Referral Hospital
P. O. Box 419
Mbeya - Tanzania

Dr. Godlove F. Mbwanji
CHAIRPERSON
Mbeya Medical Research and Ethics Review Committee

cc: The Chairperson; National Health Research Ethics Review Committee; P. O. Box 9653, Dar es Salaam.
cc: RMO - Mbeya.

All Communication should be addressed to the Chairman