FACULTY OF HEALTH SCIENCES

DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH.

VIROLOGIC NON-SUPPRESSION, CLINICAL STATUS AND ASSOCIATED FACTORS AMONG CHILDREN ON FIRST-LINE ANTIRETROVIRAL THERAPY AT MBALE REGIONAL REFERRAL HOSPITAL: A CROSS-SECTIONAL STUDY.

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ABSTRACT

Background: Virologic non-suppression, defined in this study as a viral load of at least 1,000 copies/mL at six months after ART initiation, increases the risk of HIV disease progression, opportunistic infections, drug resistance and mortality. Children living with HIV continue to experience lower viral suppression than adults. This study determined virologic non-suppression at six months, described six-month clinical status and assessed associated factors among children aged 2 to 14 years receiving first-line ART at the Chronic Care Clinic of Mbale Regional Referral Hospital.

Methods: A retrospective cross-sectional study was conducted using medical records of children aged 2 to 14 years on first-line antiretroviral therapy at Mbale Regional Referral Hospital Chronic Care Clinic. All eligible records were included. Data were abstracted on socio-demographic characteristics, antiretroviral therapy history, adherence, clinical status, opportunistic infections, nutritional status, and viral load outcomes. Virologic non-suppression was defined as viral load of at least 1,000 copies per millilitre after at least six months of antiretroviral therapy. Data were analysed using descriptive statistics and modified Poisson regression. Adjusted prevalence ratios, 95% confidence intervals, and p values were reported.

Results: A total of 274 children's records were analysed. Overall, 23.7% of the children had not achieved virological suppression after six months of antiretroviral therapy. Of the children, 49.3% were in World Health Organisation clinical stage II, while 28.8% were in stage III or IV. Opportunistic infections were documented 32.7% of children. The factors independently associated with virologic non-suppression were caregivers being relatives other than parents [adjusted prevalence ratio (aPR): 1.91; 95% confidence interval (CI): 1.11 to 3.93], poor treatment adherence [aPR: 2.92; 95% CI: 1.53 to 5.51], World Health Organization clinical stage III or IV [aPR: 1.57; 95% CI: 1.01 to 3.02], and having opportunistic infections at six months [aPR: 1.81; 95% CI: 1.05 to 3.12] at six months in

Conclusion: Virologic non-suppression was common among children on first-line antiretroviral therapy at Mbale Regional Referral Hospital. Strengthening adherence support, caregiver-centred follow-up, clinical monitoring, and timely management of opportunistic infections is critical for improving paediatric human immunodeficiency virus treatment outcomes.

Key Terms: Virologic non-suppression, Viral suppression; virological failure; immune suppression; immunological failure; viral rebound; paediatric HIV; antiretroviral therapy.

DECLARATION

I, **AKOL WALTER,** declare that this research proposal titled **"*Virologic non-response, Clinical status and associated factors among children on first-line antiretroviral therapy at Mbale Regional Referral Hospital: across-sectional study***" is my own original work and that it has not been presented to Busitema University for a similar or any other degree award.

Signature: _____ Date: 08th / July / 2026 .

APPROVAL

This is to certify that this research proposal entitled **"*Virologic non-response, Clinical status and associated factors among children on first-line antiretroviral therapy at Mbale Regional Referral Hospital: a cross-sectional study*"** has been written under my supervision, and I am satisfied with the contents therein up to this stage

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Signature: _____ **Date: 07th August 2026 .**

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DEDICATION

This dissertation is dedicated to the remarkable people whose unwavering love, encouragement, and support sustained me throughout my academic journey.

I dedicate this work to my beloved wife, Mrs Flavia Nakakande, whose patience, understanding, and steadfast support enabled me to pursue my studies. I am particularly grateful for her commitment to caring for our family during my absence.

I also dedicate this work to my beloved parents, Mr Opera Micheal and Mis Anyait Margaret, whose parental care, prayers, guidance, and sacrifices have shaped me into the person I am today.

To my beloved children, Opera Jessy, Ikinyom Christian, Aluku Austin, Akol Alvin, Anyait Audrey, and Oluka Arthur, you are precious gifts and a constant source of inspiration. May this work remind you of the value of dedication, resilience, and the pursuit of education.

With profound love and gratitude, I dedicate this work to you all.

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LIST OF ABBREVIATIONS/ACRONYMS.

ART – Antiretroviral Therapy

HIV – Human Immunodeficiency Virus

MOH – Ministry of Health

NNRTI – Non-Nucleoside Reverse Transcriptase Inhibitors

UNAIDS – Joint United Nations Programme on HIV/AIDS

CCC – Chronic Care Clinic

MRRH – Mbale Regional Referral Hospital

WHO – World Health Organisation

PMTCT – Prevention of Mother-to-Child Transmission

CD4+ – Cluster of Differentiation 4 (T-helper cell marker)

VL – Viral Load

OI – Opportunistic Infection

CCC - Chronic Care Clinic Mbale

OPERATIONAL DEFINITIONS

Virological Suppression: Reduction of HIV viral load in a patient on ART to <1,000 copies/mL of plasma, in line with WHO guidelines.

Virological Failure: Inability to achieve or maintain suppression of viral replication to <1,000 copies/mL after at least six months of ART, confirmed by two consecutive viral load measurements.

Immune Response: The recovery or improvement of immune function in HIV-infected individuals on ART, typically measured by an increase in CD4+ T-cell counts.

Immunological Failure: The failure of the immune system to show adequate and sustained recovery in CD4+ T-lymphocyte counts despite being on ART for at least 6 months**.** According to WHO criteria, immunological failure is present if, after a minimum of 6 months on ART and confirmed on two consecutive CD4 measurements (taken 3–6 months apart)

Viral Rebound: A confirmed return of detectable HIV viral load ≥1,000 copies/mL in a patient who had previously achieved virological suppression.

Opportunistic Infections (OIs): Infections that occur more frequently or are more severe in individuals with weakened immune systems, including tuberculosis, Pneumocystis pneumonia, candidiasis, and others, as classified by the WHO.

Adherence to ART: The extent to which a person's medication-taking behaviour aligns with agreed-upon recommendations from a healthcare provider; the WHO defines optimal adherence as taking≥95% of prescribed doses.

First-line ART: The initial combination of antiretroviral drugs recommended by WHO usually consists of two nucleoside reverse transcriptase inhibitors (NRTIs) + one NNRTI or integrase inhibitor.

CHAPTER ONE: INTRODUCTION

1.1 Background

Antiretroviral therapy (ART) has substantially improved the survival, growth, immune recovery, and quality of life of children living with HIV. Its primary treatment goal is to suppress HIV replication to levels below the detectable or clinically significant threshold. Sustained virologic suppression allows the immune system to recover, reduces the occurrence of opportunistic infections, slows HIV disease progression, and lowers the risk of death among children living with HIV (Getaneh et al., 2025; World Health Organization, 2021b). Therefore, achieving and maintaining virologic suppression is an important indicator of successful ART among children.

Despite the benefits and increased availability of ART, virologic suppression among children remains below global targets. Globally, in 2024, only 54% of the estimated 1.7 million children living with HIV were receiving ART compared with 74% of adults; this figure reflects treatment coverage and should be distinguished from the third 95 target, which concerns viral suppression among people receiving ART (UNAIDS, 2025). Paediatric virologic outcomes vary by treatment regimen, adherence and clinical characteristics, and non-suppression remains an important challenge in sub-Saharan Africa and East Africa (Chouraya et al., 2019; Ferrand et al., 2016; Mukuku et al., 2025). In Uganda, national programme data from June 2023 indicated viral suppression of 87% among children receiving ART, implying approximately 13% virologic non-suppression, while facility-based studies have reported substantially higher levels in selected paediatric populations (Uganda Aids Commission, 2024; Nabukeera et al., 2021; Maena et al., 2021).

Several measures have been introduced to improve the identification and management of virologic non-suppression among children. These include routine viral load monitoring, differentiated HIV service delivery, enhanced adherence counselling, use of more effective ART regimens, and point-of-care viral load testing. Point-of-care testing can shorten the time between specimen collection, receipt of results, and initiation of appropriate clinical action (Ainembabazi et al., 2024). Uganda has expanded paediatric ART services and routine viral load monitoring in line with national and international HIV treatment recommendations. However, virologic suppression among children remains inadequate.

Virologic non-suppression has serious clinical and public health consequences. Continued viral replication weakens immune recovery and increases the likelihood of progression to advanced HIV disease. Affected children may experience recurrent opportunistic infections, poor growth, malnutrition, delayed development, repeated hospital admission, and increased mortality. Persistent viral replication may also lead to the development of HIV drug resistance, treatment failure, and the need to change to more expensive and less accessible alternative ART regimens (Bisson et al., 2020; World Health Organization, 2021a). These consequences increase the demand for health services, raise treatment costs, and reduce the future treatment options available to children living with HIV.

Virologic non-suppression among children is influenced by interacting child, caregiver, treatment, and health service factors. Reported factors include younger age, late ART initiation, advanced WHO clinical stage, low CD4 count, poor nutritional status, opportunistic infections, poor treatment adherence, missed clinic appointments, treatment interruption, inappropriate ART regimens, and HIV drug resistance (Ferrand et al., 2016). Because younger children depend on caregivers for medication administration and clinic attendance, caregiver availability, relationship to the child, treatment knowledge, and consistency of care may also affect virologic outcomes (Nabukeera et al., 2021). At the health service level, delayed viral load testing, delayed return of results, limited adherence support, medicine stock shortages, and inadequate follow-up may contribute to persistent non-suppression (Ferrand et al., 2016; Mukuku et al., 2025; Nabukeera et al., 2021).

Evidence on virologic non-suppression among younger children in Eastern Uganda remains limited. Existing evidence from Mbale has mainly focused on adolescents, yet Mbale Regional Referral Hospital receives children from urban, peri-urban and rural communities across the Eastern Region, where distance to care, caregiver dependence and continuity of treatment may influence outcomes (Maena et al., 2021; Uganda Aids Commission, 2024). The unresolved question was therefore the magnitude of virologic non-suppression at six months, the clinical status of these children, and the factors associated with non-suppression among children aged 2 to 14 years receiving first-line ART at the Chronic Care Clinic. This study addressed that local evidence gap to support paediatric HIV monitoring, adherence support and clinical care at Mbale Regional Referral Hospital.

1.2 Problem Statement

Despite expanded access to antiretroviral therapy and routine viral load monitoring, virologic non-suppression remains an important paediatric HIV treatment problem in Uganda. National programme data show that children have lower viral suppression than the overall population receiving ART, while studies from Ugandan paediatric cohorts have also reported substantial non-suppression (Uganda Aids Commission, 2024; Nabukeera et al., 2021). In Mbale, available published evidence has largely focused on adolescents rather than younger children, leaving an important local evidence gap.

Virologic non-suppression exposes children to persistent immune suppression, progression to advanced HIV disease, recurrent opportunistic infections, poor growth, drug resistance, hospital admission, and death. It may also require children to change to more expensive and less accessible alternative ART regimens. The problem may be increased by poor treatment adherence, missed clinic appointments, psychosocial difficulties, delayed disclosure of HIV status, and dependence on caregivers for medication administration and clinic attendance. Children receiving care at Mbale Regional Referral Hospital may experience additional challenges because the hospital serves urban, peri-urban, and rural populations, some of whom travel long distances to obtain HIV care.

However, the available evidence from Mbale has mainly focused on adolescents and does not adequately describe virologic non-suppression, clinical status, and associated factors among children aged 2 to 14 years receiving first-line ART. Consequently, the magnitude of the problem and the child, caregiver, treatment, and clinical factors contributing to virologic non-suppression in this population are not sufficiently understood. This study addressed this gap by determining the prevalence of virologic non-suppression, describing the clinical status, and assessing factors associated with virologic non-suppression among children receiving first-line ART at Mbale Regional Referral Hospital.

1.3 Objective

1.3.1 Main objective

To determine virologic non-suppression at six months after ART initiation, describe clinical status at six months, and assess associated factors among children on first-line antiretroviral therapy attending the Chronic Care Clinic, Mbale Regional Referral Hospital.

1.3.2 Specific Objectives

1. To determine the prevalence of virologic non suppression at six months after initiation of first line antiretroviral therapy among children attending the Chronic Care Clinic, Mbale Regional Referral Hospital.
2. To describe the clinical status at six months after initiation of first line antiretroviral therapy among children attending the Chronic Care Clinic, Mbale Regional Referral Hospital.
3. To determine the factors associated with virologic non-suppression among children on first-line ART at the Chronic Care Clinic, Mbale Regional Referral Hospital.

1.4 Research Questions

1. What is the prevalence of virologic non-suppression at six months after initiation of first-line ART among children attending the Chronic Care Clinic, Mbale Regional Referral Hospital?
2. What is the clinical status at six months after initiation of first-line ART among children attending the Chronic Care Clinic, Mbale Regional Referral Hospital?
3. What are the factors associated with virologic non-suppression among children on first-line ART at the Chronic Care Clinic, Mbale Regional Referral Hospital?

1.5 Justification

Achieving sustained virologic suppression in children on first-line antiretroviral therapy remains a significant challenge, particularly in resource-limited settings. Children face unique barriers to treatment success, including adherence difficulties, limited access to paediatric formulations, and psychosocial vulnerabilities. At Mbale Regional Referral Hospital, the Chronic Care Clinic serves a large paediatric population, yet little is known about virologic non-suppression and the factors influencing outcomes in this context.

Understanding these patterns is crucial for designing effective interventions, improving adherence support, optimising viral suppression, and enhancing long-term health outcomes. The findings from this study will provide evidence to inform clinical decision-making, strengthen paediatric HIV care programs, and guide strategies that can be applied in similar high-burden settings

1.6 Scope of the Study

1.6.1 Time scope

This study reviewed medical records of children living with HIV who were initiated on first line antiretroviral therapy at the Chronic Care Clinic of Mbale Regional Referral Hospital between January 2019 and December 2025. This period covered changes in paediatric HIV treatment recommendations in Uganda, including the adoption of dolutegravir based first line antiretroviral therapy from 2020 (Ministry of Health Uganda, 2018; Ministry of Health Uganda, 2020).

1.6.2 Geographical scope

The study was conducted at the Chronic Care Clinic (CCC) of Mbale Regional Referral Hospital, located in Mbale District, Eastern Uganda. Mbale Regional Referral Hospital is a major public health facility that serves as a referral and specialized care centre for 14 surrounding districts, including Bududa, Sironko, Manafwa, and Pallisa, among others. It also offers similar services to adults. The clinic caters for a diverse paediatric population with varying socio-demographic backgrounds from several districts in eastern Uganda, making it an ideal setting to examine virologic non-suppression and identify factors associated with treatment outcomes in children on first-line ART.

1.6.3 Content scope

This study focused on virologic non-suppression, clinical status and associated factors among children living with HIV receiving first-line antiretroviral therapy at the Chronic Care Clinic of Mbale Regional Referral Hospital. The analysis included viral load Suppression or non-suppression, clinical indicators such as growth and opportunistic infections, and key factors influencing treatment response, including demographic, clinical, and adherence-related variables. Data were drawn from routinely collected medical records, capturing both baseline characteristics at ART initiation and follow-up measurements over the treatment period of the first six months.

The study was limited to children aged 2-14 years on first-line ART and excluded adults, children on second-line therapy, and conditions not routinely documented in clinic records. By concentrating on paediatric ART outcomes and associated factors within this high-burden setting, the study aimed to generate actionable insights for improving treatment effectiveness and guiding targeted interventions.

1.7 Conceptual Framework

This conceptual framework presents the interaction between the background factors (socio-demographic factors), proximate factors (patient factors) and the outcome variables (Kokeb & Degu, 2016).

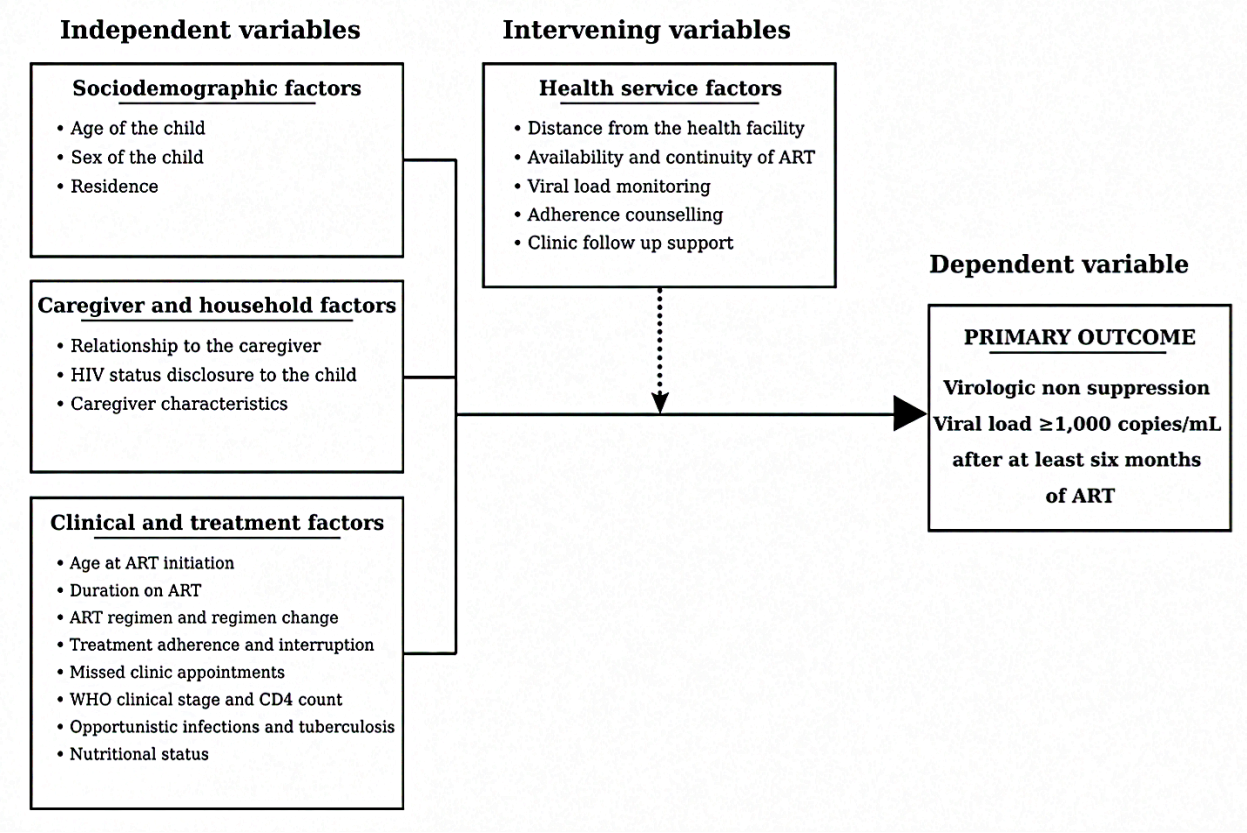

Figure 1: Conceptual framework.

The conceptual framework illustrates the relationship between child sociodemographic factors, caregiver and household factors, clinical and treatment factors, health service access factors, and virologic non-suppression among children receiving first-line ART. Child characteristics, including age, sex, and residence, may influence access to treatment and the ability to achieve virologic suppression. Caregiver stability, relationship to the child, and disclosure of HIV status may affect medication administration, clinic attendance, and adherence support. Clinical and treatment factors, including ART regimen, treatment adherence, treatment interruption, WHO clinical stage, CD4 count, opportunistic infections, and nutritional status, may directly influence virologic outcomes. Health service access factors, particularly distance from the health facility,

viral load monitoring, continuity of ART supply, and follow-up support, may also affect sustained treatment and virologic suppression. The principal outcome was virologic non-suppression, defined as a viral load of at least 1,000 copies/mL after at least six months of ART.

CHAPTER TWO: LITERATURE REVIEW

2.1 Virologic non-suppression in Children on ART

Virologic suppression is a cornerstone of successful antiretroviral therapy (ART) and a key determinant of long-term health outcomes in children living with HIV (CLHIV). Achieving viral suppression, typically defined as a viral load below 1000 copies/mL, reduces the risk of HIV disease progression, opportunistic infections, and HIV transmission. Sustained suppression also improves overall survival and quality of life for children on ART (W. M Han et al., 2021; Ferrand et al., 2016; Mukuku et al., 2025). Effective virologic control reflects not only the efficacy of the ART regimen but also adherence, timely initiation of therapy, and the capacity of the healthcare system to provide ongoing monitoring and support.

Antiretroviral therapy suppresses HIV replication by blocking critical stages of the viral life cycle. Nucleoside or nucleotide reverse transcriptase inhibitors inhibit reverse transcription, while non-nucleoside reverse transcriptase inhibitors act on reverse transcriptase through a different binding mechanism. Integrase strand transfer inhibitors such as dolutegravir prevent integration of viral DNA into the host genome, and protease inhibitors interfere with maturation of newly produced virions. Combination ART therefore reduces the production of replication-competent virus, progressively lowers plasma viral load and permits immune recovery. The durability of this effect depends on use of an effective regimen, adequate drug exposure and sustained adherence (World Health Organization, 2021a; Ferrand et al., 2016; Mukuku et al., 2025).

Despite widespread ART availability, many children face challenges in achieving optimal virologic suppression. Globally, only about 40% of children on ART attain sustained viral suppression, which is substantially lower than rates reported in adult populations (Ferrand et al., 2016; W. M Han et al., 2021). In Latin America, viral suppression among children ranges from 60% to 78%, with lower rates observed in those receiving older or suboptimal regimens (Chouraya et al., 2019). In Asia, delayed ART initiation, co-infections, and adherence difficulties significantly affect outcomes (Ferrand et al., 2016). In sub-Saharan Africa, the prevalence of virologic non-suppression among children ranges from 10% to 35%, with higher rates reported among older children and adolescents (Mukuku et al., 2025). In Uganda, despite scale-up of paediatric ART and routine viral load monitoring, approximately 13% of children fail to achieve viral suppression (Uganda Aids Commission, 2024).

2.2 Clinical status among children on first-line ART

Clinical status among children receiving ART can be assessed using WHO clinical stage, nutritional status, opportunistic infections, tuberculosis status, anaemia, CD4 count, functional status, hospital admission, and mortality. ART improves clinical status by suppressing viral replication, supporting immune recovery, and reducing HIV related illness. In Kampala, Tukei et al. (2013) found that the mean CD4 percentage among infants increased from 23% at ART initiation to 30% after six months and 36% after 24 months. Similarly, a study conducted in Arua reported sustained immunological recovery, with a median CD4 increase of 206 cells/mm³ among children aged five years and above after 12 months of ART (Ahoua et al., 2011). These findings demonstrate that ART can improve immune and clinical outcomes, although the level of recovery may depend on the child's clinical condition at treatment initiation.

Advanced HIV disease and malnutrition remain common among Ugandan children receiving HIV care. Before initiating antiretroviral therapy, children enrolled in a multicentre study conducted in central, western and Eastern Uganda presented with poor clinical status; 50.3% were in World Health Organisation clinical stage III, 21.8% were in stage IV, 14.1% were underweight, and 55.1% had anaemia (Huibers et al., 2019). Tukei et al. (2013) similarly reported that 55.6% of infants in Kampala had advanced HIV disease, while 64.3% were underweight at treatment initiation. After six months of ART, underweight reduced from 65.4% to 30.8% and wasting reduced from 33.8% to 13.8%, although stunting did not improve significantly (Tukei et al., 2013). More recently, Ahmed et al. (2026) found that 46.0% of children attending ART clinics in Bushenyi District, western Uganda had undernutrition, including 36.6% with stunting, 24.4% with underweight, and 10.9% with wasting. Undernutrition was associated with high viral load, low CD4 count, missed ART doses, shorter ART duration, and opportunistic infections (Ahmed et al., 2026).

Opportunistic infections and other clinical complications may persist despite ART, particularly among children who initiate treatment with advanced disease. In Central Uganda, tuberculosis was diagnosed among 11.9% of infants at or shortly after ART initiation, while malnutrition, pneumonia, anaemia, tuberculosis, and oral candidiasis were documented among children who experienced poor clinical outcomes (Tukei et al., 2013). In Northwestern Uganda, most children initiated ART with advanced clinical and immunological disease, and deaths occurred mainly

during the first six months of treatment (Ahoua et al., 2011). Advanced WHO clinical stage was also associated with late virologic failure in the multicentre Ugandan cohort that included children from Mbale (Huibers et al., 2019). Collectively, these studies show that viral load alone does not provide a complete assessment of treatment response. Regular monitoring of WHO clinical stage, nutritional status, opportunistic infections, tuberculosis, CD4 count, and other clinical outcomes remains necessary. However, evidence describing these indicators among children receiving first-line ART at Mbale Regional Referral Hospital remains limited, which justified their assessment in the current study.

2.3 Factors Associated with Virologic Non-Suppression among Children on First-Line ART

2.3.1 Treatment-Related Factors

Adherence to ART can be assessed using several complementary methods, including caregiver or patient self-report, pill counts, pharmacy refill records, appointment keeping, medication possession measures and, where available, electronic monitoring. Each approach has limitations; self-report may overestimate adherence because of recall or social desirability, while pill counts and refill records show medicine availability but do not confirm ingestion. In routine paediatric HIV care, combining clinician assessment with refill history, pill counts and caregiver reports provides a pragmatic assessment of adherence, although misclassification remains possible (World Health Organization, 2021a; Nabukeera et al., 2021; Ferrand et al., 2016).

Paediatric first-line ART regimens have also changed over time. Earlier Ugandan treatment guidance relied substantially on nevirapine, efavirenz and ritonavir-boosted lopinavir-based combinations according to age, weight and clinical circumstances. From 2020, dolutegravir was progressively adopted as the preferred anchor medicine for eligible children and adolescents, and subsequent guidance expanded DTG-based first-line treatment across paediatric weight bands. Second-line treatment is selected after confirmed treatment failure and depends on the child's previous regimen, age, weight and resistance considerations. These therapeutic transitions are important when interpreting virologic outcomes across records from 2019 to 2025 because children were exposed to different first-line regimen eras (Ministry of Health Uganda, 2018; Ministry of Health Uganda, 2020; World Health Organization, 2021a).

Patient-related factors are critical determinants of both virologic and clinical outcomes among children receiving first-line antiretroviral therapy (ART). Understanding these factors is essential for designing interventions to improve viral suppression, immune recovery, and overall child health. The duration of antiretroviral therapy (HAART) and the timing of treatment initiation are among the most critical determinants of treatment success in children living with HIV. The period a child has been on HAART influences both virologic and immunologic outcomes, as well as overall growth and development. Children with longer exposure to ART generally achieve more robust viral suppression, better CD4+ T-cell recovery, and enhanced physical growth compared to those who were recently initiated on therapy (W. M Han et al., 2021; Mukuku et al., 2025; Ferrand et al., 2016). Prolonged exposure to HAART allows for sustained viral control, which in turn reduces chronic immune activation and the risk of opportunistic infections (Mukuku et al., 2025; Ferrand et al., 2016; W. M Han et al., 2021).

Early initiation of ART, particularly within the first year of life, has consistently been shown to improve long-term clinical and virologic outcomes. In a prospective cohort study in Cameroon, children aged 0–5 years who began HAART within the first 12 months of life demonstrated higher rates of sustained viral suppression over five years, with 66.8% maintaining viral loads below 1000 copies/mL (Ndongo et al., 2021). The study further reported that early treatment facilitated faster immune reconstitution, evidenced by greater increases in CD4+ counts, and improved growth trajectories compared to children who started ART later in childhood. Similarly, in South Africa, children who initiated ART early were less likely to experience opportunistic infections, anaemia, and growth faltering, emphasising the protective effect of timely therapy initiation (Violari et al., 2008).

The total length of time on therapy also interacts closely with adherence patterns. In Uganda, a longitudinal study of children aged 1 month to 12 years receiving HAART for at least five years revealed that longer duration on treatment was associated with better physical growth, improved neurodevelopmental outcomes, and more stable immunologic recovery (Nabukeera et al., 2021). However, the study highlighted that extended duration without consistent adherence could paradoxically result in virologic non-suppression and the emergence of drug resistance, underscoring that duration alone is insufficient to ensure optimal outcomes.

The interplay between treatment duration and the timing of initiation is particularly important. Children who begin HAART early and maintain high adherence over time are more likely to achieve sustained virologic suppression and improved immunologic responses, thereby reducing morbidity and mortality (Ferrand et al., 2016; Ndongo et al., 2021; Violari et al., 2008; W. M Han et al., 2021). Conversely, children who initiate therapy late, especially beyond the first year of life or during advanced stages of HIV disease, often experience delayed viral suppression, lower CD4 recovery, and higher susceptibility to opportunistic infections (Mukuku et al., 2025; Ferrand et al., 2016; Ndongo et al., 2021). These findings collectively highlight the importance of not only initiating ART promptly but also ensuring sustained adherence over the long term to maximise therapeutic benefits in paediatric populations.

2.3.2 CD4+ Count and Immune Status

CD4+ count remains a critical marker of immune function in children living with HIV (CLHIV), especially in settings where viral load monitoring may be less frequent. A low baseline CD4+ count at the time of ART initiation is associated with an increased risk of opportunistic infections, poor growth outcomes, and higher mortality rates. This underscores the importance of early and consistent monitoring of CD4+ levels to guide clinical management and improve health outcomes. In a study conducted in rural North-Central Uganda, children with advanced HIV disease and a baseline CD4+ count ≤50 cells/μL had a significantly higher risk of mortality compared to those with higher CD4+ counts. The adjusted hazard ratio for mortality in this group was 1.91 (95% CI: 1.08–3.39), highlighting the prognostic value of CD4+ count in this population (Bwogi et al., 2025).

Evidence from Uganda indicates that baseline CD4 count may predict subsequent virologic response among children initiating ART. In a multicentre prospective cohort involving 316 children from Kampala, Fort Portal, and Mbale, baseline immunodeficiency was associated with threefold higher odds of early virologic failure, OR 3.3, 95% CI: 1.1 to 10.2 (Huibers et al., 2019). The study further found that virologic failure occurred in 38.8% of the children during 48 months of follow-up, with most failures occurring within the first 24 months. These findings suggest that children initiating ART with low CD4 counts may have poorer virologic outcomes and require closer viral load monitoring, adherence support, and timely clinical review.

However, the relationship between baseline CD4 count and virologic suppression has not been consistent across Ugandan studies. At the Joint Clinical Research Centre in Kampala, children who developed virologic failure had a lower median baseline CD4 count than those who did not fail, 241 cells/mm³ compared with 313 cells/mm³, although the difference was not statistically significant (Sebunya et al., 2013). Similarly, Tukei et al. (2013) found that baseline CD4 percentage did not independently predict virologic suppression among infants receiving ART in Kampala, despite 71.8% achieving suppression after six months (Tukei et al., 2013). These contrasting findings indicate that baseline CD4 count provides important information about immune status but should not be used alone to predict virologic suppression. Viral load monitoring remains necessary because some children may have high CD4 counts despite ongoing viral replication.

Furthermore, research in Ethiopia's Amhara region found that children with a CD4+ count below a certain threshold had a 2.34 times greater hazard of developing opportunistic infections compared to those with higher counts. This emphasises the need for vigilant monitoring and timely intervention in children with low CD4+ levels (Mekonnen et al., 2025).

Routine CD4+ assessments complement viral load testing by providing insights into immune system recovery and guiding clinical management decisions, such as prophylaxis for opportunistic infections and nutritional support interventions. In settings where viral load monitoring may be infrequent or unavailable, CD4+ count serves as a valuable tool for assessing immune competence and making informed treatment decisions(Bwogi et al., 2025; Huibers et al., 2019; Mekonnen et al., 2025; Tukei et al., 2013).

2.3.3 Nutritional Status

Malnutrition remains a prevalent and critical factor influencing treatment outcomes in children living with HIV (CLHIV). Undernourished children exhibit slower immune recovery, reduced response to antiretroviral therapy (ART), and heightened vulnerability to opportunistic infections (Admasu et al., 2024; Kassaw et al., 2024; Mmbaga et al., 2024; Nabukeera et al., 2021). Nutritional deficiencies, particularly in protein and micronutrients, compromise the body's ability to repair immune cells and respond effectively to viral replication.

A study conducted by (Admasu et al., 2024) in Ethiopia demonstrated that malnutrition significantly impairs the immune response in CLHIV. The researchers found that children with inadequate nutritional status had lower CD4+ counts and higher viral loads, indicating poor immune function and increased disease progression. This underscores the importance of addressing nutritional deficiencies to enhance the effectiveness of ART.

Similarly, research by Kassaw et al. (2024) highlighted the deleterious effects of undernutrition on mortality rates among HIV-infected children. The study revealed that malnourished children had a higher risk of death due to disease progression, emphasising the need for integrated nutritional care in the management of HIV.

Integrating nutritional support, including therapeutic feeding programs and micronutrient supplementation, has been shown to improve both virologic suppression and clinical outcomes. For instance, a study in Malawi found that prompt initiation of ART combined with therapeutic food led to improved growth and immune recovery in malnourished children (Mmbaga et al., 2024). This approach not only addresses the immediate nutritional needs but also supports the long-term health and development of CLHIV.

In Uganda, a prospective study conducted among children aged 1 month to 12 years receiving HAART for at least five years revealed that those with better nutritional status at ART initiation experienced improved growth outcomes and reduced incidence of opportunistic infections (Nabukeera et al., 2021). The study highlighted the critical role of adequate nutrition in optimising the benefits of ART.

2.3.4 Comorbidities and Opportunistic Infections

Children living with HIV may experience tuberculosis, anaemia, chronic diarrhoea, malaria, malnutrition, and other opportunistic infections alongside HIV. These conditions can increase nutritional requirements, weaken immunity, complicate medication schedules, and affect treatment adherence. Some medicines used to manage comorbidities may also interact with ART or increase adverse effects, making sustained viral suppression more difficult (Wudu et al., 2025; Tukei et al., 2013; Ahoua et al., 2011; Huibers et al., 2019). Therefore, the relationship between comorbidities and virologic outcomes may operate through immune suppression, poor treatment tolerance, increased pill burden, and interruption of ART.

Ugandan evidence demonstrates a relationship between anaemia and virologic suppression. In a study of 257 HIV infected children in rural Uganda, 57.6% had anaemia before ART initiation. After three months of ART, viral suppression was significantly lower among children with anaemia than among those without anaemia, 53.4% compared with 86.7%, respectively (Ruhinda et al., 2012). Anaemia was also associated with advanced WHO clinical stage and low CD4 percentage. These findings suggest that anaemia may identify children with greater disease severity and an increased risk of poor virologic response. However, because anaemia can result from HIV disease, nutritional deficiency, malaria, opportunistic infections, or ART toxicity, its underlying cause should be assessed when interpreting its relationship with viral suppression.

Tuberculosis and other opportunistic infections also contribute to poor clinical outcomes among children receiving ART. In Kampala, tuberculosis was diagnosed among 11.9% of infants at or shortly after ART initiation, while tuberculosis, pneumonia, oral candidiasis, anaemia, and malnutrition were documented among infants who experienced poor outcomes during follow-up (Tukei et al., 2013). A study in Arua similarly reported that most children initiated ART with advanced disease, and early deaths were partly attributed to delayed diagnosis and treatment of tuberculosis, pneumonia, and other severe infections (Ahoua et al., 2011). More recent evidence from Bushenyi District showed that opportunistic infections were strongly associated with undernutrition among children receiving ART, while undernutrition was also associated with high viral load and low CD4 count (Ahmed et al., 2026). Collectively, these findings support integrated screening and management of comorbidities, nutritional problems, adherence, and viral load to improve paediatric ART outcomes(Tukei et al., 2013; Ahoua et al., 2011; Huibers et al., 2019; Wudu et al., 2025).

2.3.5 Sociodemographic and Caregiver Factors

The term “children” is used differently across paediatric HIV studies and may include infants, younger children, older children and adolescents. This distinction is important because medication formulations, caregiver dependence, disclosure, schooling, autonomy and adherence challenges change with developmental stage. In this review, age ranges reported by individual studies are therefore interpreted in relation to the study population, while the present study specifically focused on children aged 2 to 14 years.

Socio-demographic characteristics significantly influence both virologic suppression and clinical outcomes among children living with HIV (CLHIV) on first-line antiretroviral therapy (ART). These factors shape treatment adherence, access to healthcare services, psychosocial support, and ultimately the effectiveness of therapy in achieving long-term health outcomes(Mukuku et al., 2025; W. M Han et al., 2021; Nabukeera et al., 2021).

Age is a key determinant of ART response in children. Infants and younger children often achieve rapid viral suppression and robust immunologic recovery when ART is initiated early, largely due to a relatively preserved immune system and lower viral reservoir (W. M Han et al., 2021; Ferrand et al., 2016; Mukuku et al., 2025).However, older children and adolescents frequently face higher rates of virologic non-suppression and treatment interruptions. This is often attributed to behavioural challenges, evolving psychosocial needs, and the transition from caregiver-managed to self-managed treatment. Adolescence is a critical period where adherence may be compromised by stigma, peer pressure, and increasing autonomy, leading to increased susceptibility to opportunistic infections and growth deficits (Ferrand et al., 2016; W. M Han et al., 2021; Mukuku et al., 2025).These findings depict the need for age-specific adherence support interventions to optimise virologic and clinical outcomes.

Sex differences in treatment outcomes have been documented, although results are sometimes inconsistent across studies. Evidence suggests that male children are more likely to experience virologic non-suppression compared with females, potentially due to differences in adherence patterns, health-seeking behaviour, and biological variations in immune recovery (Mukuku et al., 2025; Nabukeera et al., 2021; W. M Han et al., 2021) Understanding these differences is critical for designing interventions that target sex-specific barriers and ensure equitable treatment outcomes.

The occupation, socio-economic status, and educational level of caregivers are critical determinants of paediatric ART outcomes. Caregivers engaged in informal or labour-intensive employment may face challenges such as limited time, financial constraints, or lack of transportation, which can hinder their ability to supervise medication intake, attend regular clinic appointments, and provide consistent adherence support (Nabukeera et al., 2021; Tutlam et al., 2024; J. Maena et al., 2021). These limitations increase the risk of virologic non-suppression, delayed immune recovery, and poorer clinical outcomes among children living with HIV.

Conversely, caregivers with stable employment and sufficient financial resources are better positioned to ensure uninterrupted ART adherence, timely clinic visits, and access to essential healthcare services. They can also provide nutritional support, psychosocial care, and supplementary interventions that enhance both virologic and clinical outcomes (Tutlam et al., 2024; Nabukeera et al., 2021; J. Maena et al., 2021). For example, a study in Uganda demonstrated that children whose caregivers had stable jobs and higher socio-economic status were significantly more likely to achieve sustained viral suppression and improved growth parameters (J. Maena et al., 2021).

Caregiver education further influences treatment outcomes by shaping knowledge, attitudes, and practices regarding HIV care. Caregivers with higher levels of education are more likely to understand the importance of strict adherence, recognise early signs of opportunistic infections, and implement recommended nutritional and preventive measures. In contrast, low caregiver literacy or limited health knowledge has been linked to missed doses, delayed clinic attendance, and increased rates of virologic non-suppression (Mukuku et al., 2025; Nabukeera et al., 2021; J. Maena et al., 2021).

Disclosure of HIV status is a critical psychosocial determinant influencing treatment adherence and outcomes. Children who are aware of their HIV status generally demonstrate higher adherence, improved engagement with healthcare providers, and better understanding of the importance of ART, leading to enhanced viral suppression and clinical stability (Joel Maena et al., 2021; Nabukeera et al., 2021; Mukuku et al., 2025). Conversely, delayed or non-disclosure can lead to confusion, treatment resistance, and inconsistent adherence, increasing the risk of opportunistic infections and growth impairment.

Effective disclosure strategies tailored to the child's age and cognitive development are therefore essential components of comprehensive HIV care (Joel Maena et al., 2021; Nabukeera et al., 2021; Mukuku et al., 2025).

A methodological limitation across much of the available evidence is the use of cross-sectional analyses, which can identify associations but cannot establish whether clinical deterioration preceded virologic non-suppression or resulted from it. Retrospective record-based studies additionally depend on the completeness and consistency of routine documentation. These limitations require cautious interpretation of relationships between adherence, clinical status and viral load (Nabukeera et al., 2021; Maena et al., 2021; Ferrand et al., 2016).

Overall, the literature demonstrates that paediatric virologic non-suppression is shaped by treatment, adherence, clinical, caregiver and health-service factors. However, evidence specifically describing younger children receiving first-line ART at Mbale Regional Referral Hospital remains limited, particularly during the period of transition towards DTG-based paediatric regimens. Previous local work has focused more on adolescents and has not simultaneously described six-month clinical status and examined associated caregiver, treatment and clinical factors in children aged 2 to 14 years. This constituted the specific knowledge and operational gap addressed by the present study.

CHAPTER THREE: METHODS

3.1 Study Design

This was a retrospective cross-sectional record review. Existing medical records for children who had initiated first-line ART between January 2019 and December 2025 were reviewed, and the principal study outcomes and follow-up clinical variables were assessed at the six-month point after ART initiation. The design was selected because it allowed estimation of the prevalence of virologic non-suppression and examination of associated factors using routinely collected historical records without prospectively following participants. Because exposure and outcome information were analysed from a defined record-review assessment point, temporal sequence could not be established for all associated factors; the findings were therefore interpreted as associations rather than causal effects.

3.3 Study Area

The study was conducted at the Chronic Care Clinic of Mbale Regional Referral Hospital, a public tertiary referral and teaching hospital in Mbale City, Eastern Uganda. The hospital serves Mbale City and surrounding districts and receives both urban and rural referrals. The Chronic Care Clinic provides HIV testing, ART initiation and refills, clinical review, adherence counselling, nutritional assessment, tuberculosis screening, management of opportunistic infections, viral load monitoring and psychosocial support. The clinic serves a large mixed-age HIV population, including children and adolescents, through a multidisciplinary team.

Clinical and treatment information is routinely documented in ART cards, individual patient files, clinic registers and electronic medical records. Viral load information is recorded in the viral load register and electronic records, while medicine dispensing and refill information is available from pharmacy records. Patient records are retrieved using clinic identification numbers. For this study, information was cross-checked across these sources; where discrepancies occurred, the source closest to the date of the clinical event was used and unresolved discrepancies were reviewed with the principal investigator and the Chronic Care Clinic team.

3.4 Study Population

The target population comprised children aged 2 to 14 years living with HIV and receiving first-line ART in Eastern Uganda. The accessible population comprised children aged 2 to 14 years whose care was provided at the Mbale Regional Referral Hospital Chronic Care Clinic and whose medical records were available for the January 2019 to December 2025 review period. The study population consisted of eligible records from this accessible population that contained the required six-month viral load and clinical information.

The 2-14-year age range was selected to focus on children managed within paediatric HIV care while excluding infants, whose diagnostic, formulation and early-treatment pathways differ substantially, and older adolescents who increasingly experience adolescent-specific transition and self-management issues. The selected range also matched the routinely available paediatric records needed to assess six-month treatment outcomes.

3.5 Eligibility Criteria

3.5.1 Inclusion criteria

Medical records were included if they belonged to children aged 2 to 14 years who attended the Chronic Care Clinic at Mbale Regional Referral Hospital, initiated first-line ART between January 2019 and December 2025, completed at least six months of ART, and had a documented viral load result and the required clinical and treatment information for the six-month assessment.

33.5.2 Exclusion criteria

Medical records of children transferred into the clinic already receiving ART from another facility, where baseline treatment information could not be verified. Medical records with missing data on the main outcome variable, namely viral load result at or after 6 months of ART.

3.6 Sampling procedure

A census sampling approach was used. All available medical records that met the eligibility criteria were retrieved and screened; therefore, no systematic or consecutive sampling interval was applied. This approach maximised the available information and ensured that the final sample was not dependent on selection of a subset of eligible records.

3.7 Sample Size Estimation

The minimum sample size required was estimated using the modified Kish Leslie formula (1965).

$$n = \frac{Z^2 \cdot p \cdot (1 - p)}{E^2}$$

Where n was the required minimum sample size,

- Z was the standard normal value corresponding to a 95% confidence level, 1.96,
- p was the estimated prevalence of virologic non-suppression among children receiving ART, 23%, based on a previous Ugandan study conducted at the Joint Clinical Research Centre (Nabukeera et al., 2021).
- E was the desired precision of 5%.

$$n = \frac{1.96^2 x 0.23 x (1 - 0{,}23)}{0.05^2}$$

$$n = 272.18$$

Therefore, the minimum sample size required for estimating the prevalence of virologic non-suppression was 273 medical records.

For Objective 2, which described clinical status, the Kish Leslie formula for a single proportion was also applied using the proportion of children reported in WHO clinical stage IV in a Ugandan multicentre paediatric cohort, 21.8%, with a 95% confidence level and 5% precision (Huibers et al., 2019). This gave a minimum sample size of approximately 262 records. The final analytic sample of 274 records therefore exceeded the minimum required for this objective.

For the objective of assessing factors associated with virologic non-suppression, the sample size was calculated using the formula for comparing two independent proportions (Kish, 1965). Nabukeera et al. (2021) reported virologic non-suppression among 47.0% of children who initiated ART at 0 to 4 years and 19.3% of those who initiated ART at 5 to 9 years. Using these proportions, a 95% confidence level, 80% statistical power, and an equal ratio between the two groups, the minimum sample size was 90 records. After allowing 10% for incomplete records, the required sample size was increased to 100 medical records.

The larger calculated sample size was therefore 273 records. However, because the study used census sampling, all 312 eligible medical records available at the Chronic Care Clinic were screened. Of these, 38 records were excluded because they did not have eligible viral load results. Therefore, 274 medical records were included in the final analysis. This exceeded the minimum sample size required for both the prevalence and associated factors objectives.

3.8 Data Collection and Study Variables.

Data were collected through a retrospective review of routinely available medical records of children aged 2 to 14 years who had initiated first-line ART at Mbale Regional Referral Hospital. Eligible children were first identified from the electronic medical records system using age, ART regimen, date of ART initiation, and duration on treatment. The viral load register was then reviewed to confirm that each child had a documented viral load result after at least six months of ART. After confirmation of eligibility, the corresponding ART card and patient clinical file were retrieved using the clinic identification number. Information that was incomplete in the ART card or clinical file was verified using the appointment register, laboratory register, viral load register, and pharmacy dispensing records. Where information differed between records, the source closest to the date of the clinical event was used, and unresolved discrepancies were reviewed with the principal investigator before data entry. This sequence ensured consistent identification of eligible records and complete extraction of clinical, treatment, and viral load information.

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Data abstraction was conducted by the principal investigator and three research assistants. The principal investigator was a qualified medical doctor pursuing a Master of Medicine in Paediatrics and Child Health at Busitema University. The research assistants were registered nurses and clinical officers with at least a diploma in a health-related discipline and experience in HIV care or medical record review. The team was trained on the study objectives, eligibility criteria, data sources, variable definitions, confidentiality and use of Kobo Collect. The principal investigator supervised abstraction and resolved documentation uncertainties by referring to original records and consulting the Chronic Care Clinic team where necessary.

The main outcome variable was virologic non-suppression at six months after ART initiation, defined as a viral load of at least 1,000 copies/mL. Children with a viral load below 1,000 copies/mL at the six-month assessment were classified as virally suppressed. Clinical status at six months was described using documented WHO clinical stage, nutritional status, opportunistic infection status, tuberculosis status, CD4 information where available, functional status and history of hospital admission. Independent variables included child, caregiver, treatment and clinical characteristics, with follow-up variables aligned to the six-month assessment wherever applicable.

To ensure data quality, research assistants were trained on the data abstraction process, interpretation of clinical records, and use of Kobo Collect. The tool was pretested on selected records before actual data collection, and necessary adjustments were made. The principal investigator then supervised the process, reviewed completed entries daily, verified unclear or inconsistent information against the original records and gave some technical interpretation.

3.9 Data Quality Control

The research team was trained on the study protocol, eligibility criteria, data sources, variable definitions, data abstraction procedures, confidentiality, and use of Kobo Collect. The data abstraction tool was pretested using medical records that were not included in the final analysis, and identified problems were corrected before data collection. Validation checks, required fields, and skip patterns were incorporated into Kobo Collect to minimise missing and inconsistent entries. The principal investigator reviewed submitted records daily and verified incomplete or inconsistent information against the original medical records. Any unresolved discrepancies were discussed with the Chronic Care Clinic team before the record was included in the final dataset.

After data collection, the dataset was checked for completeness, duplicate entries, invalid values, and internal inconsistencies before analysis.

3.10 Measurements

Virologic non-suppression was the primary outcome and was defined as a viral load of at least 1,000 copies/mL at the six-month assessment after ART initiation. A viral load below 1,000 copies/mL at the same assessment point was classified as virologic suppression. Viral load results and dates were obtained from the viral load register, ART card, clinical file or electronic medical record.

WHO clinical stage was obtained from the clinical assessment documented by the attending clinician at six months after ART initiation and recorded as stage I, II, III or IV. For analysis, stages I and II were classified as early disease, while stages III and IV were classified as advanced disease. Baseline information was retained only as descriptive historical information where available and was not substituted for the six-month assessment.

Nutritional status was assessed using the classification documented at six months after ART initiation. Where MUAC was available, children were classified according to the documented clinic category as normal, moderate acute malnutrition or severe acute malnutrition. Where only a binary clinical classification was available, nutritional status was recorded as malnutrition present or absent. The six-month record was used consistently for the main analysis.

Treatment adherence at six months after ART initiation was obtained from the clinician's assessment documented on the ART card or clinical file and was informed by available pill counts, pharmacy refill information and caregiver report. Adherence was classified as good when at least 95% of prescribed doses were taken, moderate when 85% to 94% were taken, and poor when less than 85% were taken. Missed clinic appointments were measured from documented scheduled visits during the first six months of treatment.

Opportunistic infection status was obtained from clinician-documented diagnoses at the six-month assessment. Tuberculosis, pneumonia, oral candidiasis and zoster were retained as specific diagnosed conditions. Diarrhoea, cough and fever were treated as documented clinical symptoms or conditions and were not classified as opportunistic infections on their own. CD4 information and functional status were extracted for the six-month assessment where available.

Age at ART initiation was calculated from date of birth and ART initiation date. Duration on ART was calculated to the six-month viral load assessment. ART regimen was recorded at initiation and at six months, and regimen change was recorded when at least one medicine in the initial ART regimen had changed, together with the documented reason. This allowed the analysis to account descriptively for therapeutic changes occurring during the 2019 to 2025 period. Treatment interruption, residence, caregiver relationship, HIV status disclosure and distance from the health facility were extracted as documented in the records.

3.11 Data Analysis

Data were exported from Kobo Collect to Microsoft Excel for initial cleaning and subsequently imported into Stata version 18.0 for analysis. Data cleaning included checks for completeness, duplicate entries, missing values, out-of-range values, inconsistent responses and logical errors. Virologic non-suppression was coded as 1 for a viral load of at least 1,000 copies/mL at six months after ART initiation and 0 for a viral load below 1,000 copies/mL at the same assessment point.

Sociodemographic, caregiver, clinical, and treatment characteristics were summarised as Categorical variables and presented using frequencies and percentages. Continuous variables were summarised using means and standard deviations when normally distributed or medians and interquartile ranges when skewed. The characteristics included age, sex, residence, relationship to the caregiver, distance from the health facility, age at ART initiation, duration on ART, ART regimen, adherence, treatment interruption, missed clinic appointments, WHO clinical stage, opportunistic infections, CD4 count, and nutritional status.

The prevalence of virologic non-suppression was calculated by dividing the number of children with a viral load of at least 1,000 copies/mL by the total number of children included in the analysis. It was presented as a percentage with its corresponding 95% confidence interval. The number and proportion of children who achieved virologic suppression were also reported.

Clinical status at six months after ART initiation was summarised using descriptive statistics. WHO clinical stage, nutritional status, tuberculosis status, opportunistic infection status, functional status, hospital admission and available CD4 information were presented using the six-month assessment. Denominators were reported for variables with missing information so that the extent of missing data was transparent.

To determine factors associated with virologic non-suppression, bivariable and multivariable modified Poisson regression with robust standard errors was used to estimate prevalence ratios. Variables with $p<0.20$ at bivariable analysis, together with variables considered clinically important from previous literature, were considered for the multivariable model. Adjusted prevalence ratios, 95% confidence intervals and exact p values were reported. Regimen, duration on ART, adherence and other candidate factors were evaluated within the same model-building framework, while variable-specific denominators were retained where data were incomplete.

3.12 Ethical Considerations

Ethical approval and waiver of consent were obtained from the Busitema University Research and Ethics Committee and administrative clearance from Mbale Regional Hospital to work with the patient files. Personal identifiers were not collected, and all extracted data were stored securely and accessed only by the research team.

CHAPTER FOUR: RESULTS

4.1 Participants flow chart

During the records review period, which covered January 2019 to December 2025, a total of 312 medical records were retrieved. Of the 312 medical records assessed for eligibility, 38 were excluded; 10 had missing essential clinical data, 22 involved children who transferred out before completing six months of treatment, and six had no documented viral load result after six months of antiretroviral therapy. Consequently, 274 medical records were included in the final analysis. Figure 2.

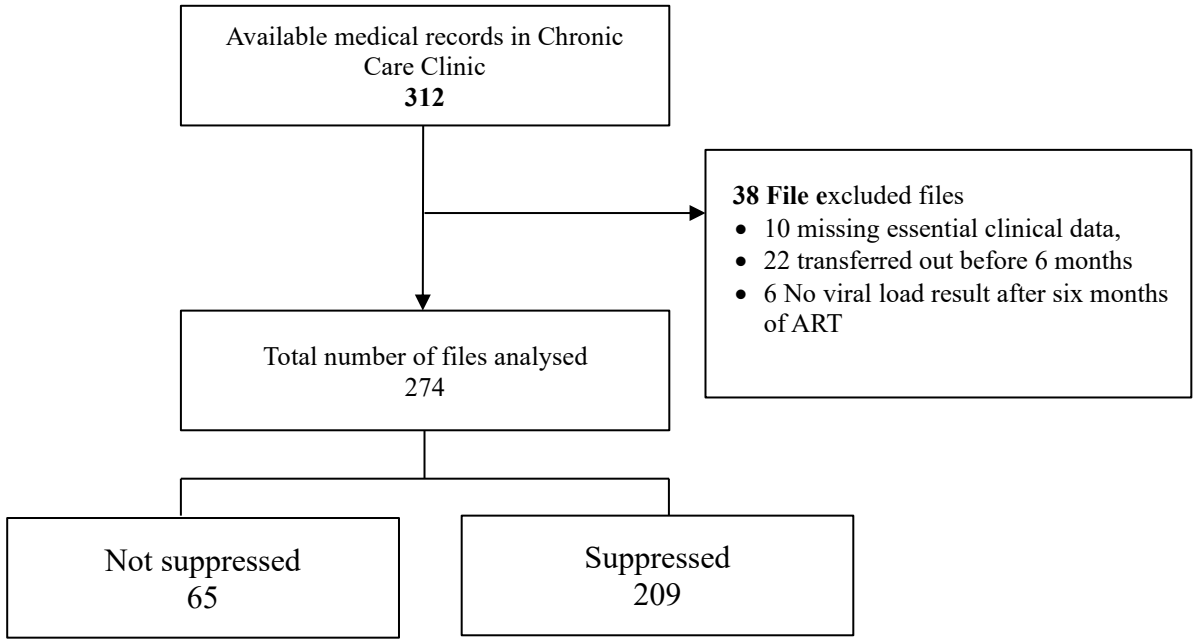

Figure 2: Participants flow chart

4.2 Sociodemographic characteristics of children on first-line ART

A total of 274 children's medical records were included in the analysis. Among the enrolled children, 50.0% (137/274) were initiated on ART at 2 to 4 years of age, 31.8% (87/274) at 5 to 9 years, and 18.2% (50/274) at 10 to 14 years. Slightly more than half (51.1%, 140/274) were male.

More than half of the children (58.4%, 160/274) lived more than 5 km from the health facility; nearly half (47.1%, 129/274) lived in households with 4 to 5 members. Most caregivers (82.8%, 227/274) were living with HIV. Among the children, 39.1% (107/274) were cared for by the mother

alone, 37.6% (103/274) by both parents, 17.5% (48/274) by other relatives, and 5.8% (16/274) by the father alone (Table 1).

Table 1: Sociodemographic characteristics of children on first-line ART

Variable	Frequency (N = 274)	Percentage
Age at ART initiation (Years)		
2 to 4	137	50.0
5 to 9	87	31.8
10 to 14	50	18.2
Sex		
Male	140	51.1
Female	134	48.9
Residence		
Urban	108	39.4
Rural	166	60.6
Distance from facility		
5 km or less	114	41.6
More than 5 km	160	58.4
Number of household members		
1 to 3	123	44.9
4 to 5	129	47.1
6 or more	22	8.0
Caregiver HIV status		
Positive	227	82.8
Negative	25	9.1
Unknown	22	8.0
Relationship with caregiver		
Both parents	103	37.6
Mother alone	107	39.1
Father alone	16	5.8
Other relatives	48	17.5

4.3 ART and treatment related characteristics

The mean weight of the children at six months was 18.5 kg (standard deviation 8.3), while the median mid upper arm circumference was 15.0 cm (interquartile range of 13.0 to 17.0 cm). Among the enrolled children, 23.7% (65/274) were initiated on abacavir, lamivudine and dolutegravir (ABC/3TC/DTG), 23.4% (64/274) on abacavir, lamivudine and efavirenz (ABC/3TC/EFV), 7.3% (20/274) on abacavir, lamivudine and nevirapine (ABC/3TC/NVP), 22.6% (62/274) on

zidovudine, lamivudine and nevirapine (AZT/3TC/NVP), and 23.0% (63/274) on zidovudine, lamivudine and ritonavir boosted lopinavir (AZT/3TC/LPV/r).

A total of 85.8% (235/274) of the enrolled children had good treatment adherence, 9.5% (26/274) had moderate adherence, and 4.7% (13/274) had poor adherence. A regimen change was recorded for 16.8% (46/274) of the children. Among those whose regimen was changed, 65.2% (30/46) changed because a new drug became available. Treatment interruption was recorded for 14.2% (39/274). Among the enrolled children, 31.0% (85/274) missed at least one scheduled clinic appointment. CD4-positive T lymphocyte count was not presented because it was not consistently documented in the medical records reviewed. (Table 2).

Table 2: Antiretroviral therapy, treatment, and selected clinical characteristics of children receiving first-line antiretroviral therapy

Characteristic	Frequency (N = 274)	Percentage (%)
ART regimen at initiation		
ABC/3TC/DTG	65	23.7
ABC/3TC/EFV	64	23.4
ABC/3TC/NVP	20	7.3
AZT/3TC/NVP	62	22.6
AZT/3TC/LPV/r	63	23.0
Current ART regimen		
ABC/3TC/DTG	102	37.2
ABC/3TC/EFV	51	18.6
ABC/3TC/NVP	18	6.6
AZT/3TC/NVP	53	19.3
AZT/3TC/LPV/r	50	18.2
Treatment adherence after six months		
Good	235	85.8
Moderate	26	9.5
Poor	13	4.7
History of ART regimen change		
Yes	46	16.8
No	228	83.2
Reason for ART regimen change (N = 46)		
Toxicity or side effects	2	4.3
Tuberculosis diagnosis	6	13.0
New drug available	30	65.2
Drug stockout	6	13.0
Clinical failure	1	2.2

Virologic failure	1	2.2
Treatment interruption history		
Yes	39	14.2
No	235	85.8
Missed clinic appointment		
No missed appointment	189	69.0
At least one missed appointment	85	31.0
Tuberculosis among records assessed for specific infections (N = 90)		
Yes	25	27.8
No	65	72.2
Nutritional status based on recorded MUAC (N = 263)		
Normal	214	81.4
Moderate acute malnutrition	33	12.5
Severe acute malnutrition	16	6.1

***ABC**, abacavir; **3TC**, lamivudine; **DTG**, dolutegravir; **EFV**, efavirenz; **NVP**, nevirapine; **AZT**, zidovudine; **LPV/r**, ritonavir-boosted lopinavir. **ART**, antiretroviral therapy; **MUAC,** mid upper arm circumference. Mid upper arm circumference measurements were available for 263 children because 11 records had no documented measurements. Tuberculosis status was analysed among 90 children whose medical records contained sufficient information on specific infections. Nutritional status based on mid upper arm circumference was assessed among 263 children because 11 records had no documented mid upper arm circumference measurements.*

4.4 Prevalence of virologic non-suppression among children on first-line ART

Overall, 76.3% (209/274) of the enrolled children achieved virological suppression, while 23.7% (65/274; 95% CI: 19.0% - 29.1%) had virological non-suppression (Figure 3).

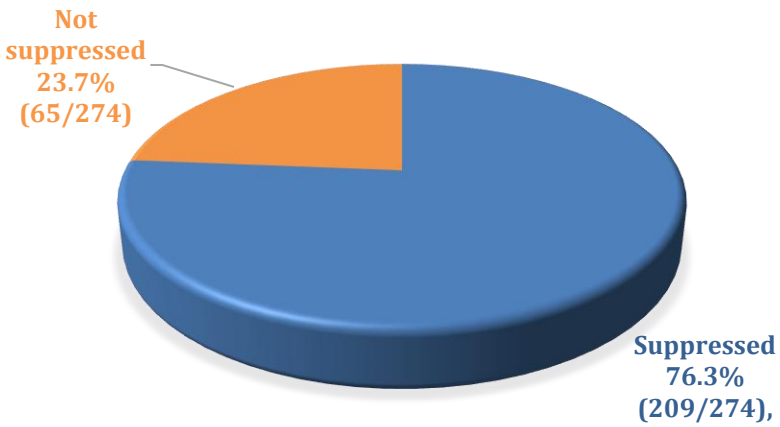

Figure 3: Prevalence of virologic non-suppression among children on first line ART

4.5 Clinical status among children on first-line ART

At six months after antiretroviral therapy initiation, 21.9% (60/274) of the children were in World Health Organisation clinical stage I, 49.3% (135/274) were in stage II, and 28.8% (79/274) were in stage III or IV. Among the 263 children with a recorded mid upper arm circumference, 81.4% (214/263) had normal nutritional status, 12.5% (33/263) had moderate acute malnutrition, and 6.1% (16/263) had severe acute malnutrition.

Opportunistic infection status at six months was available for 272 children, of whom 32.7% (89/272) had a clinician-documented opportunistic infection. Among records with specific conditions documented, cough, tuberculosis, diarrhoea, fever, zoster, pneumonia and oral thrush were recorded. Cough, diarrhoea and fever are reported as clinical symptoms or conditions and are not classified as opportunistic infections on their own. The corresponding frequencies are presented in Table 3.).

Table 3: Clinical status of children six months after initiation of first-line ART

Clinical characteristic	Frequency (n)	Percentage (%)
WHO clinical stage (N = 274)		
Stage I	60	21.9
Stage II	135	49.3
Stage III or IV	79	28.8
Nutritional status based on MUAC (N = 263)		
Normal	214	81.4
Moderate acute malnutrition	33	12.5
Severe acute malnutrition	16	6.1
Opportunistic infection at six months (N = 272)		
Yes	89	32.7
No	183	67.3
Specific documented conditions/symptoms at six months (N = 89)*		
Pneumonia	3	3.3
Tuberculosis	25	27.8
Documented diarrhoea symptom	15	16.7
Documented cough symptom	49	54.4
Documented fever symptom	10	11.1

Zoster	4	4.4
Oral thrush	3	3.3
Malnutrition recorded as a clinical condition	4	4.4
Functional status at 6 months		
Playing	197	71.9
Working	54	19.7
Ambulatory	21	7.7
Bedridden	2	0.7

Notes: **More than one specific condition could be recorded for the same child; therefore, the percentages do not total 100%.* ***Abbreviations:*** *ART, antiretroviral therapy; MUAC, mid upper arm circumference; WHO, World Health*

4.6 Factors associated with virologic non-suppression

4.6.1 Bivariable analysis

4.6.1.1 Sociodemographic factors associated with virologic non-suppression

At bivariable analysis, the socio-demographic factors associated with virologic non-suppression were residence, distance from the health facility, household size and human immunodeficiency virus (HIV) status of caregiver. Associations were expressed as crude prevalence ratios (cPRs) with 95% confidence intervals (CIs). Children living in rural areas had 2.17 times the prevalence of virologic non-suppression compared with children living in urban areas (cPR = 2.17, 95% CI: 1.29–3.66; p = 0.004). Similarly, children living more than 5 km from the health facility had twice the prevalence of virologic non-suppression compared with those living within 5 km (cPR 2.01; 95% CI 1.22–3.31; p = 0.006). Children from households with at least six members had a higher prevalence of virologic non-suppression than those from households with one to three members (cPR 1.86, 95% CI 1.07–3.24; p = 0.027). Children whose caregivers' HIV status was unknown also had a higher prevalence than those with HIV positive caregivers (cPR 2.06, 95% CI 1.23–3.47; p = 0.006) (Table 4).

Table 4: Bivariable analysis of sociodemographic factors associated with virologic non-suppression

Variable	Virologic non-suppression		cPR (95% CI)	P value
	Suppressed n (%)	Not suppressed n (%)		
Age at ART initiation				
2 to 4 years	105 (50.2)	32 (49.2)	1	
5 to 9 years	64 (30.6)	23 (35.4)	1.13 (0.71–1.80)	0.601

10 to 14 years	40 (19.1)	10 (15.4)	0.86 (0.46–1.61)	0.630
Sex				
Male	101 (48.3)	39 (60.0)	1	
Female	108 (51.7)	26 (40.0)	0.70 (0.45–1.08)	0.104
Residence				
Urban	93 (44.5)	15 (23.1)	1	
Rural	116 (55.5)	50 (76.9)	2.17 (1.28–3.66)	0.004
Distance from the health facility				
≤ 5 km	97 (46.4)	17 (26.2)	1	
> 5 km	112 (53.6)	48 (73.8)	2.01 (1.22–3.31)	0.006
Household size				
1-3 members	93 (44.5)	30 (46.2)	1	
4-5 members	104 (49.8)	25 (38.5)	0.79 (0.50–1.27)	0.337
≥6 members	12 (5.7)	10 (15.4)	1.86 (1.07–3.24)	0.027
Caregiver HIV status				
Positive	177 (84.7)	50 (76.9)	1	
Negative	20 (9.6)	5 (7.7)	0.91 (0.40–2.06)	0.818
Unknown	12 (5.7)	10 (15.4)	2.06 (1.23–3.47)	0.006
Relationship with caregiver				
Both parents	81 (38.8)	22 (33.8)	1	
Mother alone	84 (40.2)	23 (35.4)	1.01 (0.60–1.69)	0.981
Father alone	12 (5.7)	4 (6.2)	1.17 (0.46–2.95)	0.739
Other relatives	32 (15.3)	16 (24.6)	1.56 (0.90–2.69)	0.110

4.6.1.2 ART and treatment-related factors associated with virologic non-suppression

The antiretroviral therapy and treatment-related factors associated with virologic non-suppression were antiretroviral therapy regimen at initiation, treatment adherence, history of antiretroviral therapy regimen change, treatment interruption and missed clinic appointment. Children initiated on zidovudine, lamivudine and nevirapine had 2.38 times the prevalence of virologic non-suppression compared with those initiated on abacavir, lamivudine and dolutegravir (cPR 2.38, 95% CI 1.28–4.42; p = 0.006). Compared with children with good adherence, those with moderate adherence had 5.27 times the prevalence of virologic non-suppression (cPR 5.27, 95% CI 3.70–7.51; p < 0.001), while those with poor adherence had 4.02 times the prevalence (cPR 4.02, 95% CI 2.38–6.79; p < 0.001). Children with a history of antiretroviral therapy regimen change had approximately twice the prevalence of virologic non-suppression compared with those without a regimen change (cPR 2.05, 95% CI 1.33–3.15; p = 0.001). Children with a history of treatment interruption had 3.53 times the prevalence of virologic non-suppression compared with those

without a treatment interruption (cPR 3.53, 95% CI 2.43–5.12; p < 0.001), while children who missed at least one clinic appointment had 1.91 times the prevalence compared with those who did not miss an appointment (cPR 1.91, 95% CI 1.26–2.89; p = 0.002) (Table 5).

Table 5: Bivariable analysis of ART and treatment related factors associated with virologic non-suppression

Variable	Virologic non-suppression		cPR (95% CI)	P value
	Suppressed n (%)	Not suppressed n (%)		
ART regimen at initiation				
ABC/3TC/DTG	54 (25.8)	11 (16.9)	1	
ABC/3TC/EFV	50 (23.9)	14 (21.5)	1.29 (0.64–2.63)	0.479
ABC/3TC/NVP	16 (7.7)	4 (6.2)	1.18 (0.42–3.31)	0.750
AZT/3TC/NVP	37 (17.7)	25 (38.5)	2.38 (1.28–4.42)	0.006
AZT/3TC/LPVr	52 (24.9)	11 (16.9)	1.03 (0.48–2.21)	0.936
Current ART regimen				
ABC/3TC/DTG	77 (36.8)	25 (38.5)	1	
ABC/3TC/EFV	41 (19.6)	10 (15.4)	0.80 (0.42–1.54)	0.502
ABC/3TC/NVP	15 (7.2)	3 (4.6)	0.68 (0.23–2.02)	0.487
AZT/3TC/NVP	33 (15.8)	20 (30.8)	1.54 (0.95–2.50)	0.081
AZT/3TC/LPVr	43 (20.6)	7 (10.8)	0.57 (0.27–1.23)	0.152
Treatment adherence after six months				
Good	199 (95.2)	36 (55.4)	1	
Moderate	5 (2.4)	21 (32.3)	5.27 (3.70–7.51)	<0.001
Fair or poor	5 (2.4)	8 (12.3)	4.02 (2.38–6.79)	<0.001
Treatment adherence, Binary				
Good	199 (95.2)	36 (55.4)	1	
Fair or poor	10 (4.8)	29 (44.6)	4.85 (3.41–6.91)	<0.001
History of ART regimen change				
No	182 (87.1)	46 (70.8)	1	
Yes	27 (12.9)	19 (29.2)	2.05 (1.33–3.15)	0.001
Treatment interruption history				
No	194 (92.8)	41 (63.1)	1	
Yes	15 (7.2)	24 (36.9)	3.53 (2.43–5.12)	<0.001
Missed clinical appointment				
No missed appointment	154 (73.7)	35 (53.8)	1	
Missed appointment	55 (26.3)	30 (46.2)	1.91 (1.26–2.89)	0.002

4.6.1.3 Clinical factors associated with virologic non-suppression

The clinical factors associated with virologic non-suppression were nutritional status, World Health Organisation clinical stage, opportunistic infection at six months, tuberculosis, pneumonia, recorded cough and functional status. Associations were expressed as crude prevalence ratios (cPRs) with 95% confidence intervals (CIs). Children with moderate acute malnutrition had approximately twice the prevalence of virologic non-suppression compared with those with normal nutritional status (cPR 2.02, 95% CI 1.26–3.24; p = 0.004). Children in World Health Organisation clinical stage III or IV had 2.79 times the prevalence of virologic non-suppression compared with those in stage I (cPR 2.79, 95% CI 1.45–5.37; p = 0.002). Children with an opportunistic infection at six months had 3.51 times the prevalence of virologic non-suppression compared with those without an opportunistic infection (cPR 3.51, 95% CI 2.27–5.43; p < 0.001). Among the 90 records assessed for specific infections, children with tuberculosis had a higher prevalence of virologic non-suppression compared with those without tuberculosis (cPR 1.66, 95% CI 1.09–2.55; p = 0.019). Pneumonia was also associated with virologic non-suppression, while recorded cough was inversely associated with virologic non-suppression; however, these estimates should be interpreted cautiously because they were based on a small subgroup. Ambulatory children had 3.85 times the prevalence of virologic non-suppression compared with children recorded as playing (cPR 3.85, 95% CI 2.66–5.57; p < 0.001) (Table 6).

Table 6: Bivariable analysis of clinical factors associated with virologic non-suppression

Variable	Virologic non-suppression		cPR (95% CI)	P value
	Suppressed n (%)	Not suppressed n (%)		
Nutritional status based on MUAC (N = 263)				
Normal	169 (84.9)	45 (70.3)	1	
Moderate acute malnutrition	19 (9.5)	14 (21.9)	2.02 (1.25–3.24)	0.004
Severe acute malnutrition	11 (5.5)	5 (7.8)	1.49 (0.69–3.22)	0.314
WHO clinical stage				
Stage I	51 (24.4)	9 (13.8)	1	
Stage II	112 (53.6)	23 (35.4)	1.14 (0.56–2.31)	0.724
Stage III or IV	46 (22.0)	33 (50.8)	2.78 (1.44–5.37)	0.002
Opportunistic infection (N = 272)				
No	159 (76.8)	24 (36.9)	1	
Yes	48 (23.2)	41 (63.1)	3.51 (2.27–5.43)	<0.001

Pneumonia				
No	49 (100.0)	38 (92.7)	1	
Yes	0 (0.0)	3 (7.3)	2.29 (1.80–2.91)	<0.001
Tuberculosis				
No	40 (81.6)	25 (61.0)	1	
Yes	9 (18.4)	16 (39.0)	1.66 (1.09–2.55)	0.019
Documented diarrhoea symptom				
No	42 (85.7)	33 (80.5)	1	
Yes	7 (14.3)	8 (19.5)	1.21 (0.71–2.08)	0.483
Documented cough symptom				
No	16 (32.7)	25 (61.0)	1	
Yes	33 (67.3)	16 (39.0)	0.54 (0.33–0.86)	0.009
Documented fever symptom				
No	45 (91.8)	35 (85.4)	1	
Yes	4 (8.2)	6 (14.6)	1.37 (0.78–2.41)	0.272
Zoster				
No	48 (98.0)	38 (92.7)	1	
Yes	1 (2.0)	3 (7.3)	1.70 (0.92–3.14)	0.091
Oral thrush				
No	48 (98.0)	39 (95.1)	1	
Yes	1 (2.0)	2 (4.9)	1.49 (0.65–3.42)	0.351
Functional status				
Playing	158 (75.6)	39 (60.0)	1	
Working	45 (21.5)	9 (13.8)	0.84 (0.44–1.63)	0.609
Ambulatory	5 (2.4)	16 (24.6)	3.85 (2.66–5.57)	<0.001
Bedridden	1 (0.5)	1 (1.5)	2.53 (0.61–10.39)	0.199

Notes: *Modified Poisson regression with robust standard errors was used, with each factor entered separately. MUAC was available for 263 children, opportunistic infection status for 272 children, and specific infection indicators for 90 records. Reasons for regimen change were not modelled because of sparse data.* ***Abbreviations:*** *ABC, abacavir; ART, antiretroviral therapy; CI, confidence interval; cPR, crude prevalence ratio; DTG, dolutegravir; EFV, efavirenz; HIV, human immunodeficiency virus; LPV/r, ritonavir-boosted lopinavir; MUAC, mid upper arm circumference; NVP, nevirapine; 3TC, lamivudine; WHO, World Health Organisation; AZT, zidovudine.*

4.2 Multivariable analysis for factors associated with virologic non-suppression among children on first-line ART

At multivariable analysis, the factors independently associated with virologic non-suppression were caregiver relationship, treatment adherence, World Health Organisation clinical stage and opportunistic infections at six months. Associations were expressed as adjusted prevalence ratios

(aPRs) with 95% confidence intervals (CIs). Children cared for by relatives other than both parents had 1.91 times the prevalence of virologic non-suppression compared with children cared for by both parents (aPR 1.91, 95% CI 1.11 to 3.93). Children with poor treatment adherence had 2.92 times the prevalence of virologic non-suppression compared with children with good treatment adherence (aPR 2.92, 95% CI 1.53 to 5.51). Children in World Health Organisation clinical stage III or IV had 1.57 times the prevalence of virologic non-suppression compared with children in clinical stage I (aPR 1.57, 95% CI 1.01 to 3.02). Children who had opportunistic infections at six months had 1.81 times the prevalence of virologic non-suppression compared with children who had no opportunistic infections at six months (aPR 1.81, 95% CI 1.05 to 3.12) (Table 9).

Table 6: Factors associated with virologic non-suppression among children on first-line ART

Variables	cPR (95% CI)	P-Value	aPR (95% CI)	P-Value
Residence				
Urban	1		1	
Rural	2.17 (1.28 - 3.67)	0.004	1.42 (0.52 - 3.55)	0.528
Distance from facility				
≤ 5 km	1		1	
> 5 km	2.01 (1.22 - 3.31)	0.006	1.25 (0.40 - 2.52)	0.984
Household size				
1-3 members	1		1	
4-5 members	0.82 (0.50 - 1.27)	0.338	0.86 (0.50 - 1.30)	0.374
≥6 members	1.94 (1.07 - 3.25)	0.028	0.94 (0.46 - 1.68)	0.701
Caregiver HIV status				
Positive	1		1	
Negative	1.11 (0.48 - 2.51)	0.818	0.85 (0.37 - 1.96)	0.698
Unknown	2.32 (0.92 - 5.64)	0.077	1.01 (0.39 - 2.79)	0.931
Relationship with caregiver				
Both parents	1		1	
Mother alone	1.15 (0.59 - 1.67)	0.981	0.87 (0.47 - 1.31)	0.351
Father alone	1.91 (1.46 - 3.93)	0.042	1.10 (0.43 - 2.70)	0.870
Other relatives	2.67 (1.90 - 3.66)	0.002	1.91 (1.11 - 3.93)	**0.007**
Treatment adherence				
Good	1		1	
Poor	4.91 (3.41 - 6.91)	<0.001	2.92 (1.53 - 5.51)	**0.001**
Missed clinical appointment				
No missed appointment	1		1	
Missed appointment	1.98 (1.26 - 2.89)	0.002	0.85 (0.46 - 1.30)	0.328
WHO clinical staging				

WHO stage I	1		1	
WHO stage II	1.16 (0.56 - 2.31)	0.725	1.16 (0.55 - 2.15)	0.809
WHO stage III or IV	2.84 (1.44 - 5.37)	0.002	1.57 (1.01 - 3.02)	**0.014**
Opportunistic infection at six months				
No	1		1	
Yes	3.52 (2.27 - 5.43)	<0.001	1.81 (1.05 - 3.12)	**0.032**
Malnutrition				
Normal	1		1	
Moderate acute malnutrition	2.19 (1.29 - 3.34)	0.003	1.10 (0.67 - 1.85)	0.678
Severe acute malnutrition	1.53 (0.71 - 3.31)	0.282	1.42 (0.74 - 2.71)	0.298
Treatment interruption history				
Yes	1		1	
No	0.30 (0.20 - 0.41)	<0.001	0.70 (0.42 - 1.27)	0.259

Table note: *cPR, crude prevalence ratio; aPR, adjusted prevalence ratio; CI, confidence interval; HIV, human immunodeficiency virus.*

CHAPTER FIVE: DISCUSSION

5.1 Prevalence of virologic non-suppression among children on first-line ART

The study found a virologic non-suppression prevalence of 23.7%, meaning that nearly one in four children on first-line ART had a viral load of at least 1,000 copies per mL. This finding suggests that although the majority of children had achieved viral suppression, a substantial proportion still had ongoing viral replication despite being on treatment. The observed prevalence of virologic non-suppression was considerably higher than the maximum of 5% implied by the third global target, which aims to achieve viral suppression among at least 95% of people receiving antiretroviral therapy (UNAIDS, 2025). This is a clinically important finding because virologic non-suppression is usually an early warning sign of poor adherence, treatment interruption, drug resistance, underdosing as children grow, delayed regimen optimisation, or inadequate follow-up after high viral load results (Afrane et al., 2021). The prevalence observed in this study is similar to a study conducted at the Joint Clinical Research Centre in Kampala that reported that 23% of HIV positive children receiving ART had virological non-suppression in Uganda (Nabukeera et al., 2021). This similarity may be due to comparable paediatric ART programme challenges in Uganda, including caregiver-dependent drug administration, missed appointments, delayed recognition of adherence problems, and persistent use of older regimens among some children (Moro et al., 2025; Nabukeera et al., 2021). Furthermore, these results are also similar to pooled estimates of a systematic review that found that close to one quarter of children on ART in sub-Saharan Africa do not achieve virological suppression (Walle et al., 2024).

This finding is lower than the 31.4% viral load non-suppression reported among adolescents in Mbale District (J. Maena et al., 2021). The difference may be due to the different populations studied; in addition to adolescents, our study also included prepubertal children. Adolescents are less likely to achieve virological suppression due to the additional adherence barriers they face, including stigma, treatment fatigue, school routines, peer influence, and transition from caregiver-supervised treatment to self-management (J. Maena et al., 2021). Furthermore, the prevalence in this study is lower than the 57.1% virologic non-suppression reported among HIV infected children in Tanzania (Mgelea et al., 2014), suggesting better viral suppression in the current study setting. This difference may be explained by improvements over time in viral load monitoring, ART regimen optimisation, paediatric HIV guidelines, and clinical follow-up. The Tanzanian study was conducted during a period when many children were still on older regimens and routine viral load

monitoring was less widely implemented, which may have allowed treatment failure to persist undetected (Mgelea et al., 2014). On the other hand, the prevalence in this study is higher than the 14.8% reported among children on ART in Bahir Dar, Ethiopia (Gelaw et al., 2021). This difference may reflect variation in programme performance, study population, adherence support systems, duration on ART, viral load follow-up practices, and health facility organisation. Programmes with stronger tracing systems, early enhanced adherence counselling, rapid regimen switching, and better caregiver engagement may achieve lower non-suppression levels (Gelaw et al., 2021; UNICEF, 2021). Overall, the 23.7% prevalence in this study shows that first-line ART is working for most children, but a sizeable minority remains at risk of disease progression, drug resistance, and future treatment failure unless adherence monitoring, high viral load follow-up, caregiver support, and timely regimen review are strengthened (Nabukeera et al., 2021; UNICEF, 2021; Walle et al., 2024).

The high prevalence of virological non-suppression in these children may be because of the unique treatment barriers that make sustained viral suppression more difficult than in adults. Children depend on caregivers for timely dosing, clinic attendance, drug refills, food support, and interpretation of treatment instructions. When caregivers are busy, economically constrained, ill, change residence, or do not fully understand ART, the child's adherence may become inconsistent, resulting in viral replication. In addition, some children may not know their HIV status, making it difficult for them to understand why daily treatment is necessary. Paediatric dosing also requires regular adjustment with growth, and any delay in dose adjustment may contribute to suboptimal drug exposure (Afrane et al., 2021).

5.2 Clinical status among children on first-line ART at the Chronic Care Clinic

At six months after antiretroviral therapy initiation, 28.8% of the enrolled children had advanced clinical disease (stage III or IV). The proportion with advanced clinical disease is interpreted as substantial because nearly three in every ten children still had stage III or IV disease after six months of treatment, when clinical improvement would ordinarily be expected. However, the burden was lower than the 38.6% with current stage III or IV disease reported among 360 children attending ART clinics in referral hospitals in Northwest Ethiopia, most of whom had been followed for at least five years (Mengist & Terefe, 2022). It was also lower than the 55.6% with stage III or IV disease at ART initiation among 91 HIV infected infants enrolled at an urban paediatric HIV

clinic in Kampala, Uganda (Tukei et al., 2013). These comparisons should be interpreted cautiously because the Ethiopian study assessed children during long term follow up, whereas the Ugandan study reported baseline status among infants; Our study was among children who had had ART for 6 months. The present study measured clinical stage only at six months and therefore cannot determine how much clinical staging changed from ART initiation.

Nutritional assessment at six months showed that 18.6% of children with a recorded mid-upper arm circumference had either moderate or severe acute malnutrition, comprising 12.5% with moderate acute malnutrition and 6.1% with severe acute malnutrition. This represents an important nutritional burden despite most children having normal mid-upper arm circumference. The finding was lower than the 30.3% overall undernutrition reported among 360 children receiving ART follow-up in Northwest Ethiopian referral hospitals (Mengist & Terefe, 2022). Nevertheless, the studies used different anthropometric measures: the present study used mid-upper arm circumference, while the Ethiopian study assessed stunting and thinness; direct comparison is therefore limited. A total of 71.9% of the children were recorded as playing and 19.7% as working, indicating that most children could participate in normal age-appropriate activities at six months. However, 7.7% were ambulatory and 0.7% were bedridden, indicating some degree of functional limitation among 8.4% of the children. Although direct comparison is limited by differences in assessment periods, a study among children receiving antiretroviral therapy in Northwest Ethiopia reported that 10.4% were bedridden at treatment initiation. The same study found that ambulatory and bedridden functional status was associated with poorer CD4-positive T lymphocyte recovery and a greater risk of mortality compared with working functional status (Getaneh et al., 2025). This suggests that the children with functional limitations in the present study represented a clinically vulnerable group requiring closer clinical assessment and follow-up. Baseline and current functional measurements were not collected; therefore, changes in functional status between antiretroviral therapy initiation, six months, and the current period could not be assessed.

Opportunistic infections were documented in 32.7% of the 272 children with available information at six months, showing that approximately one third experienced continuing clinical morbidity during early ART follow-up. This proportion was similar to the 31.6% reported among 408 children younger than 15 years receiving ART at Debre Markos Referral Hospital in Northwest Ethiopia, although those children were followed for periods ranging from 2 to 132 months

(Melkamu et al., 2020). It was also close to the 29.8% who developed at least one opportunistic infection among 409 children receiving ART in a multi-Centre retrospective cohort in Southwest Ethiopia (Admasu et al., 2024b). Among the 89 records in which specific conditions were assessed in the present study, tuberculosis accounted for 27.8%, which was comparable to the 29.8% reported at Debre Markos and 30.3% in Southwest Ethiopia (Admasu et al., 2024b; Melkamu et al., 2020). The study did not collect opportunistic infection status at ART initiation or beyond the six-month assessment. Consequently, the findings cannot establish whether ART reduced opportunistic infections in this population; they describe only the burden documented at six months.

5.3 Factors associated with virologic non-suppression among children on first-line ART

Four factors remained independently associated with virologic non-suppression at multivariable analysis: living with other relatives, fair or poor treatment adherence compared to good adherence, advanced HIV disease (World Health Organisation (WHO) clinical stage III or IV) at six months, and the presence of an opportunistic infection at six months. The findings are discussed below in relation to comparable paediatric studies. Because the clinical exposures and viral-load outcome were assessed at the six-month review only, the observed relationships are interpreted as associations and not as evidence of causation.

Children living with other relatives had a higher prevalence of virologic non-suppression than those living with both parents. Children depend on caregivers for timely medication, collection of refills, clinic attendance, food, disclosure support, and communication with health workers. Care provided by relatives may be affected by competing household responsibilities, changes in residence, limited knowledge of the child's treatment, or weaker continuity of supervision. These mechanisms could result in missed doses and inconsistent follow-up, thereby reducing the likelihood of virologic suppression (Moro et al., 2025; Nasuuna et al., 2019). This finding is consistent with evidence linking stable parental care to better treatment outcomes. In Northern Uganda, Moro et al. (2025) found that single and double orphans were more likely to have virologic non-suppression than children whose parents were alive; their qualitative findings also showed that children cared for by both parents received better support with medication reminders, treatment monitoring, transport, and clinic attendance however a Ugandan qualitative study among caregivers of virally non-suppressed children described work demands, school schedules, stigma,

transport constraints, and caregiver fatigue as barriers to consistent adherence support (Nasuuna et al., 2019). Our results are also similar to the results of a meta-analysis that found that the death of either parent was associated with approximately twice the odds of paediatric treatment failure (Getaneh et al., 2022). The present study measured relationship with the caregiver rather than orphan status; therefore, it cannot establish that parental death explains the association. Nonetheless, the findings support careful assessment of caregiving arrangements and targeted adherence support for children living with relatives.

Children with fair or poor adherence had nearly three times the prevalence of virologic non-suppression compared with those with good adherence. Inconsistent dosing reduces antiretroviral drug exposure, permits continued viral replication, and increases the likelihood of antiretroviral drug resistance (Panel on Antiretroviral & Medical Management of Children Living with, 2025). Adherence among children is particularly vulnerable because medication administration depends on caregivers, while palatability, pill burden, school attendance, disclosure, stigma, and household mobility may further interfere with daily treatment (Nasuuna et al., 2019; Panel on Antiretroviral & Medical Management of Children Living with, 2025). This finding is consistent with evidence from Ethiopia, where poor or fair adherence was associated with virologic failure (Bayleyegn et al., 2021), and with a systematic review that reported an AOR of 2.53 (95% CI: 2.03–4.97) for treatment failure among children with poor adherence (Gelaw et al., 2022). Moro et al. (2025).It did not demonstrate a statistically significant adjusted association between adherence and virologic non-suppression. Their study included only children and adolescents who had received dolutegravir-based regimens for at least six months. In contrast, the present study included children receiving several first-line regimens containing dolutegravir, efavirenz, nevirapine, or ritonavir-boosted lopinavir. Only 23.7% of the children in the present study initiated antiretroviral therapy on a dolutegravir-based regimen, although this proportion increased to 37.2% for the current regimen.

Dolutegravir-based regimens generally provide more potent viral suppression and have a higher barrier to drug resistance than the older efavirenz, nevirapine, and ritonavir-boosted lopinavir-based regimens included in the present study. Differences in regimen composition may therefore partly explain the variation in the observed association between adherence and virologic non-suppression. In contrast, the present study included children aged 2–14 years on several first-line

regimens and assessed adherence at the six-month review. Differences in age composition, regimen potency, duration on treatment, adherence measurement, and statistical power may explain the different findings. The current result therefore emphasises the need for early identification of adherence difficulties and caregiver-centred support before persistent viraemia develops.

Children in WHO clinical stage III or IV at six months had a higher prevalence of virologic non-suppression than those in stage I at six months. Advanced disease at this review may indicate incomplete clinical recovery, ongoing HIV replication, delayed recognition of treatment problems, or concurrent illness that interferes with adherence and drug absorption. Conversely, continuing viral replication may itself contribute to clinical deterioration. Since WHO stage and viral-load status were assessed at the same six-month point, the temporal direction of this relationship cannot be determined. The association is similar to findings of a multicentre study of children receiving first-line ART in Northeast Ethiopia, in which recent WHO stage III or IV predicted virologic failure (Abebe et al., 2024). This comparison is particularly relevant because that study used a post-initiation or recent clinical stage rather than only baseline stage. Nabukeera et al. (2021) likewise found that WHO stage IV was associated with non-suppression among children at the Joint Clinical Research Centre in Uganda; however, staging in that study was recorded at ART initiation, whereas the present study assessed clinical stage at six months. Thus, both studies show the same direction of association, but they describe different treatment time points and should not be interpreted as directly equivalent. The present finding indicates that children who remain in an advanced WHO stage after six months require prompt clinical review, adherence assessment, investigation for comorbid disease, and repeat viral-load management according to national guidelines.

Children who had an opportunistic infection at six months had a higher prevalence of virologic non-suppression than those without. Opportunistic infections may increase inflammation and treatment complexity, interfere with oral intake or drug absorption, and increase pill burden and the risk of drug interactions. At the same time, inadequate viral suppression weakens immune recovery and increases susceptibility to opportunistic infections (Panel on Opportunistic Infections in Children With and Exposed to HIV, 2024). Because both conditions were documented at the six-month assessment, the finding demonstrates coexistence and association but does not establish which occurred first. This result is consistent with a study from Northwest Ethiopia, where

opportunistic infections were associated with virologic failure (Bayleyegn et al., 2021). Furthermore, a systematic review and meta-analysis in also found that opportunistic infections were associated with childhood treatment failure (Gelaw et al., 2022). The finding supports integrated management in which children presenting with an opportunistic infection at the six-month visit receive timely treatment, an adherence review, assessment of possible treatment failure, and close viral-load follow-up.

Because the study used a retrospective cross-sectional record-review design, the observed relationships must be interpreted cautiously. Advanced clinical stage and opportunistic infections may contribute to poor virologic control, but persistent viral replication can also worsen immune and clinical status. The six-month assessment therefore demonstrates coexistence and association rather than temporal causation. This temporal ambiguity was considered when interpreting all associated factors.

The association between poor adherence and non-suppression is particularly important in paediatric care because medication taking depends on both the child and the caregiver. In settings similar to Eastern Uganda, adherence may be challenged by changing caregivers, caregiver fatigue, school routines, stigma, transport constraints, formulation acceptability and reliance on extended family members for treatment supervision. These contextual mechanisms provide plausible explanations for the observed association but were not directly measured in this record review and should therefore be explored prospectively.

From a policy and service-delivery perspective, the observed suppression level remains below the UNAIDS third 95 target. For Mbale Regional Referral Hospital, the findings support strengthening paediatric enhanced adherence counselling, timely viral load review, active follow-up of children with high viral loads, and targeted support for children cared for by non-parent relatives or presenting with advanced clinical disease. These actions are consistent with the need to translate routine viral load monitoring into prompt clinical action at regional referral level.

5.4 Study strength and limitations

5.4.1 Study strength

First, the study focused on children aged 2 to 14 years, a population that is often underrepresented in HIV treatment outcome studies compared to adults and adolescents. This makes the study important because children have unique treatment challenges, including dependence on caregivers,

need for age-appropriate ART formulations, changing drug doses with growth, and difficulties related to disclosure and adherence support.

Second, the study used viral load as the main outcome measure for virologic non-suppression. Viral load is a more direct and reliable indicator of ART treatment response compared to clinical or immunological indicators alone. This strengthened the validity of the findings because virologic non-suppression was measured using an objective laboratory-based outcome.

Third, the study included a relatively large number of eligible children's records from a tertiary hospital potentially including children from several parts of eastern Uganda, therefore increasing generalisability, which improved the precision of the estimates. The use of census sampling also reduced the risk of selection bias because all available eligible records that met the inclusion criteria were considered for inclusion.

Finally, the study assessed a broad range of factors, including socio-demographic, caregiver-related, treatment-related, and clinical factors. This allowed the study to examine virologic non-suppression from a comprehensive public health perspective, rather than limiting the analysis to only biological or treatment variables.

5.4.2 Limitations

This study had several limitations. First, the retrospective cross-sectional design does not establish temporal sequence or causality between associated factors and virologic non-suppression. Nevertheless, the design was appropriate for estimating prevalence and examining associations using existing clinical records at a defined six-month assessment point. Findings were therefore consistently interpreted as associations rather than causes.

Second, the study relied on routinely collected medical records, and some variables may have been incompletely or inconsistently documented. To mitigate this, information was cross-checked across ART cards, clinical files, viral load registers, appointment registers, pharmacy records and electronic medical records; unclear entries were verified against original sources, unresolved discrepancies were discussed with the Chronic Care Clinic team, and variable-specific denominators were reported where information was missing. These procedures reduced, but could not completely eliminate, information error and misclassification.

Second, treatment adherence was assessed using the clinician's adherence classification documented on the antiretroviral therapy card or in the clinical file. This classification was based on available pill counts, pharmacy refill records, and caregiver reports. Adherence was classified as good when at least 95% of the prescribed doses were taken, moderate when 85% to 94% were taken, and poor when less than 85% were taken. However, these routine measures may not fully reflect the children's actual medicine-taking behaviour and may overestimate adherence because caregivers may forget missed doses or may be unwilling to report them accurately.

Third, some important factors that could influence virologic non-suppression may not have been available in the routine records. These include household income, food security, caregiver mental health, stigma, school-related barriers, disclosure quality, drug resistance testing, and detailed ART dispensing history. Their absence may have limited the depth of explanation for some observed associations.

Finally, some historical baseline clinical information was not consistently available. To reduce variability in the principal analyses, virologic non-suppression, clinical status, adherence and other follow-up clinical variables were standardised to the six-month assessment after ART initiation wherever available. Remaining variation in routine documentation may still have introduced random measurement error, and this was considered when interpreting the findings.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The study established that virologic non-suppression among children on first-line antiretroviral therapy at the Chronic Care Clinic of Mbale Regional Referral Hospital remains an important clinical and public health concern. Nearly one in every four children had virologic non-suppression. This shows that first-line ART is achieving viral control for the majority of children, but a meaningful subgroup still has ongoing viral replication and remains at risk of disease progression, drug resistance, opportunistic infections, and eventual need for second-line ART.

Nearly a third of the enrolled children were in WHO clinical stage III or IV. Furthermore, a similar proportion had opportunistic infections at six months. This indicates that despite ART access, some children continue to experience advanced clinical disease and HIV related morbidity. The findings point to the need for stronger clinical monitoring, early identification of illness, routine nutritional assessment, tuberculosis screening, and timely management of opportunistic infections.

The study further found that virologic non-suppression was independently associated with being cared for by relatives other than the parents, poor treatment adherence, advanced HIV disease, and opportunistic infections at six months. These findings show that virologic non-suppression among children is not only a drug-related issue, but also a caregiving, adherence, and clinical care issue. Children who lack stable parental support, have poor adherence, present with advanced HIV disease, or develop opportunistic infections require closer follow-up and more intensive support. Overall, the findings highlight the need for child-centred, caregiver-centred, and clinically targeted interventions to improve viral suppression among children on first-line ART.

6.2 Recommendations

The Chronic Care Clinic should strengthen paediatric viral load follow-up and enhanced adherence counselling, with priority given to children with non-suppression, poor adherence, advanced clinical disease, opportunistic infections, and those whose treatment is supervised by relatives other than parents. High viral load results should trigger timely adherence review, clinical assessment and repeat viral load testing according to national guidance.

Mbale Regional Referral Hospital should strengthen integrated six-month clinical review for children on ART by linking viral load assessment with screening and management of opportunistic infections, nutritional assessment, tuberculosis evaluation, appointment tracking and caregiver

support. This would allow children at increased risk of poor outcomes to be identified and managed earlier.

Future research should use prospective longitudinal cohort designs to clarify the temporal relationship between adherence, caregiver factors, clinical deterioration and virologic non-suppression, and to assess treatment outcomes across evolving DTG-based paediatric regimens in Eastern Uganda.

6.3 Contribution to Knowledge

This study provides contemporary, setting-specific evidence on virologic non-suppression among children aged 2 to 14 years receiving first-line ART at Mbale Regional Referral Hospital, a regional referral setting serving both urban and rural populations in Eastern Uganda. It extends local evidence beyond adolescent-focused studies by integrating six-month viral load outcomes with clinical status, caregiver characteristics, adherence and treatment-related factors.

The findings have direct programme relevance because they identify groups requiring intensified follow-up within routine Ministry of Health paediatric HIV services, particularly children with poor adherence, advanced clinical disease, opportunistic infections and non-parent caregivers. The study also captures outcomes across a period of transition from older NNRTI and protease inhibitor-based regimens towards optimised DTG-based paediatric treatment, providing a useful baseline for future evaluation of regimen durability and viral suppression in Eastern Uganda.

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APPENDIX I: REC APPROVAL LETTER

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FACULTY OF HEALTH SCIENCES' REC

04/06/2026
To: AKOL WALTER
BusitemaUniversity

Review Type: Initial Review

BUSITEMA UNIVERSITY
FACULTY OF HEALTH SCIENCES
APPROVED VALID UNTIL
04 JUN 2027
RESEARCH & ETHICS COMMITTEE
P. O. BOX 1460, MBALE

Re:BUFHS-2026-687: VIROLOGIC NON-SUPPRESSION, CLINICAL STATUS AND ASSOCIATED FACTORS AMONG CHILDREN ON FIRST-LINE ANTIRETROVIRAL THERAPY AT MBALE REGIONAL REFERRAL HOSPITAL: ACROSS-SECTIONAL STUDY

I am pleased to inform you that at the **7th** convened meeting on **07/05/2026**, the Busitema University Faculty of Health Sciences REC meeting voted to approve the above referenced application.
Approval of the research is for the period of **04/06/2026** to **04/06/2027.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re-review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **04/06/2027** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.
6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by Busitema University Faculty of Health Sciences REC:

No.	Document Title	Language	Version Number	Version Date
1	Response to Reviewers letter	English	1.0	2026-05-19
2	Akol Walter proposal track changes	English	1.2	2026-05-19
3	Akol Walter proposal Clean copy	English	1.2	2026-05-19
4	Protocol	English	1.0	2026-03-24
5	Main Consent forms	English	1.0	2026-04-10
6	Data collection tools	English	1.0	2026-04-10

Yours sincerely,

BUSITEMA UNIVERSITY
FACULTY OF HEALTH SCIENCES
APPROVED VALID UNTIL
★ 04 JUN 2027 ★
RESEARCH & ETHICS COMMITTEE
P. O. BOX 1460, MBALE

Richard Katuramu
For: Busitema University Faculty of Health Sciences REC

APPENDIX II: ADMINISTRATIVE CLEARANCE

BUSITEMA UNIVERSITY
Pursuing Excellence

P.O.Box 236, Tororo
Gen: +256-454448842
Dir: +256-454448864
Mob: +256-782998174
Fax: +256-454448651
Email:ar@acadreg.busitema.ac.ug
Website:www.busitema.ac.ug

DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

AKOL WALTER
Walterdr2012@gmail.com

05th June 2026

Mr. Charles Okumu
Mbale RRH RDC
P/Sec Letter

To
Hospital director,
Mbale Regional Referral Hospital
Dear sir,

HOSPITAL DIRECTOR
02 JUN 2026
MBALE REGIONAL HOSPITAL
P.O. BOX 921, MBALE

RE: ADMINISTRATIVE CLEARANCE TO CONDUCT DATA COLLECTION

My name is **AKOL WALTER**, a postgraduate student pursuing a Master of Paediatrics and Child Health at Busitema University Faculty of Health Sciences. I am currently conducting a research study entitled ***"Virologic Non-Response, Clinical Status and Associated Factors among Children on First Line Antiretroviral Therapy at Mbale Regional Referral Hospital: A Cross-Sectional Study."*** The purpose of this study is to assess the prevalence of virologic non response, evaluate the clinical status, and identify factors associated with virologic non response among children receiving first line antiretroviral therapy at Mbale Regional Referral Hospital. The findings from this study are expected to contribute to improving pediatric HIV care and treatment outcomes.

I kindly request for administrative clearance and permission to conduct data collection at your facility. The study will be conducted in a manner that will not interfere with routine hospital activities or patient care services. All information collected will be treated with strict confidentiality.

I will be grateful for your support and cooperation in facilitating this research at your institution. I am available to provide any additional information that may be required.

Thank you for your consideration.

Yours faithfully,

AKOL WALTER

Principal Investigator
Department of Paediatrics and Child Health
Busitema University Faculty of Health Sciences
Mbale Campus
Email: Walterdr2012@gmail.com

APPENDIX III: ADMINISTRATIVE APPROVAL

Telephones: General Line: 039-3280584
041-4671162

E-mail: mrrhrec@gmail.com

MINISTRY OF HEALTH
MBALE REGIONAL HOSPITAL
P.O. BOX 921
Mbale – Uganda

THE REPUBLIC OF UGANDA

In any correspondence on this
Subject, please quote: MRRHREC-OUT- 231/2026 **Date:08th June 2026**

MRHREC ACCREDITED BY THE UNCST, REGISTRATION NUMBER UG-REC-011

ADMINISTRATIVE APPROVAL

To: Akol Walter
Busitema University

Principal Investigator
RE:BUFHS-2026-687:" Virologic Non-suppression, clinical status and associated factors among children on first-line antiretroviral therapy at Mbale Regional Referral Hospital: A cross-sectional study".

OFFICE OF THE CHAIRPERSON
APPROVED
APPROVED DATE EXPIRY DATE
08 JUN 2026 04 JUN 2027
MBALE REGIONAL REFERRAL HOSPITAL
RESEARCH & ETHICS COMMITTEE
(MRRH- REC)

Type:
[ ] Initial Review
[ ] Protocol Amendment
[ ] Letter of Amendment (LOA)
[ ] Continuing Review
[√] Other, Specify: Administrative approval.

Thank you for submitting the above study to **Mbale Regional Referral Hospital** for Research and Administrative clearance.

In line with MRRH-REC S.O.P # 04, I am glad to inform you that the above application, that was reviewed and approved by the **Busitema University Faculty of Health Sciences Research Ethics Committee (BUFHS-REC),** has been granted administrative permission to be carried out within **Mbale Regional Referral Hospital.**

This Administrative Approval covers the dates **(08th June 2026 to 04th June 2027)** in line with **–the BUFHS-REC approved** period.

You are responsible for fulfilling the following requirements of Administrative approval:

1. All Co-investigators and the heads of the departments from where your study will be carried out must be **informed and involved** in all aspects of this research.
2. While in the Hospital, your research activities should not interfere with the day-to-day routine activities in the respective department.
3. In the conduct of your study, you are required to adhere to the Ministry of Health and the Uganda National Council of Science and Technology Guidelines for Conduct of Research, including abiding by all reporting requirements.
4. All conditions as spelled out by REC on record **BUFHS-REC must** be adhered to, including the requirement to use only approved/stamped data collection tools and consent forms.

5. You shall be required to share a copy of your findings/ progress reports with **MRRH-REC,** including an end-of-study report upon completion.

6. That you include **Mbale Regional Referral Hospital** in your acknowledgments and in all your publications.

Yours sincerely,

OFFICE OF THE CHAIRPERSON
APPROVED
APPROVED DATE 0 8 JUN 2026 EXPIRY DATE 0 4 JUN 2027
MBALE REGIONAL REFERRAL HOSPITAL
RESEARCH & ETHICS COMMITTEE
(MRRH- REC)

Dr.Fred Bulamba, MBcHB, MMeD, cert Med Educ.
Chairperson-MRRH-REC

APPENDIX IV: WAIVER OF INFORMED CONSENT

BUSITEMA UNIVERSITY
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MBALE REGIONAL REFERRAL HOSPITAL
RESEARCH & ETHICS COMMITTEE
P.O.BOX 921, MBALE
RECEIVED
Date: 24/06/2026

Ref: BUFHS-2026-687/WIC
Date: 19 June 2026

Akol Walter
Master of Paediatrics and Child Health Student
Busitema University Faculty of Health Sciences

Dear Dr. Akol,

RE: APPROVAL OF WAIVER OF INFORMED CONSENT — PROTOCOL NO. BUFHS-2026-687 "VIROLOGIC NON-SUPPRESSION, CLINICAL STATUS AND ASSOCIATED FACTORS AMONG CHILDREN ON FIRST-LINE ANTIRETROVIRAL THERAPY AT MBALE REGIONAL REFERRAL HOSPITAL: A CROSS-SECTIONAL STUDY"

The Busitema University Faculty of Health Sciences Research Ethics Committee (BUFHS-REC) refers to your letter requesting a waiver of informed consent for the above-referenced study, Protocol No. BUFHS-2026-687, which proposes a retrospective review of routinely collected medical records of children aged 2 to 14 years initiated on first-line antiretroviral therapy at the Chronic Care Clinic of Mbale Regional Referral Hospital between January 2019 and December 2025.

The Committee has carefully considered your request and the justifications provided, including the minimal risk posed to participants given the use of de-identified, routinely collected clinical data; the impracticability of obtaining consent retrospectively from children and caregivers across a seven-year review period, some of whom may have transferred out, relocated, or been lost to follow-up; the public health and clinical significance of the study in informing improvements in paediatric HIV care; the data security and confidentiality safeguards proposed; and the absence of any anticipated adverse effect on the rights, safety, or welfare of the children whose records will be reviewed.

The Committee is satisfied that the study meets the ethical criteria for a waiver of informed consent, namely that the research involves no more than minimal risk to participants, the waiver will not adversely affect the rights and welfare of the participants, the research could not practicably be carried out without the waiver, and, where appropriate, participants will be provided with relevant information after participation.

Accordingly, the Committee hereby GRANTS a WAIVER OF INFORMED CONSENT for the conduct of the above study under Protocol No. BUFHS-2026-687, subject to the following conditions:

1. This waiver applies strictly to the retrospective review and abstraction of routinely documented clinical and treatment information from ART cards, patient clinical files, viral load registers, clinic appointment registers, and electronic medical records, as described

in the approved protocol. It does not extend to direct contact, interviews, or any additional data collection involving the children or their caregivers.

2. No names, clinic numbers, or other direct personal identifiers shall be entered into the study database. Each eligible record shall be assigned a unique study identification number, and the link between identifiers and study numbers shall be securely stored separately from the study dataset.
3. All extracted data shall be accessed only by the principal investigator and authorised members of the research team, and the electronic database shall be password protected at all times.
4. No identifying information shall appear in any analysis, report, presentation, or publication arising from this study.
5. The study shall not alter the clinical management of any patient.whose records are reviewed, and findings shall be used solely for the stated research purpose.
6. Permission for access to the relevant records shall be separately obtained from the administration of Mbale Regional Referral Hospital, where required, prior to commencement of data abstraction.
7. Any amendment to the study protocol, including any change to the scope of records or variables to be reviewed, shall be submitted to this Committee for review and approval before implementation.
8. This approval is valid for twelve (12) months from the date of this letter. Continuation beyond this period shall require submission of a continuing review report and renewal of approval by the Committee.

You are reminded that you remain responsible for ensuring that the study is conducted in accordance with the approved protocol, the conditions of this waiver, and all applicable national and institutional research ethics guidelines. Please report any deviations, breaches of confidentiality, or unanticipated problems to this Committee promptly.

We wish you success with your research.

Yours sincerely,

Dr. Katuramu Richard
Chairperson, Research Ethics Committee
Busitema University Faculty of Health Sciences (BUFHS-REC)

cc:
Hospital Director, Mbale Regional Referral Hospital
Head, Chronic Care Clinic, Mbale RRH

APPENDIX V: DATA ABSTRACTION FORM

Duration on ART	Months / Years	Derived from initiation date (Generated automatically in months and in years)
ART regimen at initiation	1. ABC/3TC/DTG 2. ABC/3TC/EFV 3. ABC/3TC/NVP 4. AZT/3TC/NVP 5. AZT/3TC/EFV	
Current ART regimen	1. ABC/3TC/DTG 2. ABC/3TC/EFV 3. ABC/3TC/NVP 4. AZT/3TC/NVP 5. AZT/3TC/EFV	Note reason for change
Treatment adherence after 6 months of initiation	1. Good 2. Moderate 3. Poor	
ART changes	1. Yes 2. No	If No skip
Reasons of change of ART regimen	1. Toxicity/side effects 2. Due to new TB 3. New Drug available 4 Drug out of stock 5. Other reasons specify 6. Clinical failure 7. Immunological failure 8. Virological failure	
Treatment interruption history	1. Yes 2. No	Duration if applicable
7. Virological non-response		

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Data Abstraction Form

Variable	Description / Response Options	Notes / Comments
A. Patient Demographics		
Study ID	Unique ID assigned by research team	
Date of Birth	DD/MM/YYYY	–
Age at ART initiation	..... (Age in years)	
Sex	1. Male 2. Female	–
Residence	1. Urban 2. Rural	
Distance from facility	1. ≤ 5km 2. > 5km	
Caregiver HIV status	1. Positive 2. Negative 3. Unknown	If documented
Relationship with the caregiver	1. Both parents 2. Mother alone 3. Father alone 4. Other relatives	
Number of members in the household	.....	
B. ART Treatment Details		
Date of ART initiation	DD/MM/YYYY	–

Viral load suppression after 6 months of in initiation	1. Suppressed 2. Not suppressed (≥1,000)	
D. Clinical Response	3.	
Weight (kg) at 6 months	……	–
Height (cm) *(If age is >5 years)*	……	
MUAC (<5 years)	cm	Nutritional status
WHO clinical stage at ART initiation at 6th month *(Select one)*	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
Opportunistic infections at 6th month	1. Pneumonia 2. TB 3. Diarrhoea 4. Cough 5. Fever 6. Zoster 7. Thrush 8. Malnutrition	
Functional status	1. Playing 2. Work 3. Ambulatory 4. Bedridden	As documented
Clinic attendance in the last 12 months	Number of visits attended	Missed appointments noted