A RETROSPECTIVE DESCRIPTIVE STUDY OF IMMUNOLOGICAL AND VIROLOGICAL PROFILES OF ADULTS WHO ACQUIRED HIV IN CHILDHOOD THROUGH MOTHER-TO-CHILD TRANSMISSION.

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DECLARATION

Student's Declaration

I declare that the work presented in this dissertation was carried out at the Children of God Relief Institute. Any information that was obtained from published work is acknowledged in the text, references, and appendices. The contents of this dissertation are entirely my original work and have not been presented for a degree or other award to any other University.

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DEDICATION

In honor of everyone who makes my life worthwhile, especially my sister Wangari, I dedicate this work.

ABSTRACT

Background: To provide optimal targeted interventions, it is important to describe the virological and immunological profiles across all subgroups of people living with HIV (PLWH). This includes special groups like adults who contracted HIV through mother-to-child transmission (MTCT). Such individuals usually acquire HIV in childhood when their immune systems are immature and still developing. The ability of the virus to adapt and evolve within the host's body in childhood, and potential viral variations, could all lead to a unique viral dynamics and modulate the course of the disease even later in adulthood. This contrasts with adults who contract HIV through other routes, such as sexual contact or intravenous drug use, where their immune systems are typically more developed. Yet, adults who contracted HIV through MTCT are understudied. Studying their immunological and virological profiles could inform optimization of their treatment Programmes.

Methods: To characterize the immunological and virological profiles of ART-treated adults who acquired HIV through MTCT, we conducted a retrospective study on secondary data that were collected from HIV-infected adults who were registered in Children of God Relief Institute (COGRI) in childhood. To maximize the study's statistical power, the study included all the COGRI participants who had their immunological and or virological profiles done in the year 2018; HIV Viral load, CD4 T cell counts, lymphocyte count, neutrophils count, and monocytes counts were retrieved from the laboratory information system. Data on potential predictors of immunological and virological failure were also retrieved, namely age, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and opportunistic infections-tuberculosis and Cryptococcal meningitis.

Results: Viral load suppression at <1,000 copies/mL was 73% (479 of 652) in ART-treated adults who acquired HIV in adulthood through MTCT, lower than that previously reported in ART-treated adults in the general population (90.6%). The median for CD4 T cell counts was 569 cells/mm^3. Median percentages for neutrophils, lymphocytes and monocytes were 45%, 45%, 5.5 %, respectively. The median AST and ALT levels were 24.45 IU/L and 17.6 IU/L, respectively.

Participants who had detectable viremia (>1,000 copies/mL) also had lower CD4 counts ($P<0.001$), lower percentages of lymphocytes ($p=0.024$) and higher percentages of monocytes ($P<0.001$) when compared to those who were viremically suppressed (=/<1,000 copies/mL). There were also notable inverse correlations between ALT and viral loads (Rho= -0.11, $p<0.05$) as well as between AST and CD4 counts (Rho= -0.12, $p<0.05$).

Discussion:The study underscores the distinct challenges faced by adults who acquired HIV through MTCT, emphasizing their unique immunological and virological profiles and the implications for their long-term health outcomes. Understanding these unique profiles is crucial for developing targeted interventions and treatment strategies that address the specific needs of this population, ultimately improving their quality of life and reducing the burden of HIV/AIDS. These differences, particularly the lower rates of viral load suppression, underscore the need for tailored treatment approaches. The disparities between this subgroup and the general adult population highlight potential gaps in our understanding and management of HIV in those with childhood-acquired infection.

Conclusion: ART-treated adults who acquired HIV in childhood through MTCT have lower rates of viral load suppression when compared to ART-treated adults who acquired HIV in adulthood. The resultant poor viral load suppression is associated with decreased CD4 counts, lowered percentages of lymphocytes and elevated percentages of monocytes, suggestive of compromised immune system and immune activation.

The study suggests clinicians should monitor and tailor therapeutic interventions for adults with HIV acquired through MTCT, with further research to understand underlying mechanisms. Health systems should prioritize capacity-building initiatives and training to improve care for these unique individuals.

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LIST OF ABBREVIATIONS AND ACRONYMS

3TC-Lamivudine

ABC-Abacavir

ALT- Alanine aminotransferase

ANC- antenatal care

ARV- antiretroviral

AST- Aspartate aminotransferase

ATV- Atazanavir

ATV/r- Atazanavir/ritonavir

AZT-Zidovudine

cART- combined antiretroviral therapy

CD4 -Cluster of Differentiation

COGRI- Children of God Relief Institute

CrAg -Cryptococcal antigen

DRT- Drug resistance testing.

DRV- Darunavir

DRV/r- Darunavir/ritonavir

DTG- Dolutegravir

D4T–Stavudine

EDTA- Ethylenediaminetetraacetic acid

EFV- Efavirenz

EMTCT- Elimination of Mother to child transmission

FTC- Emtricitabine

HAART- Highly-active Antiretroviral Therapy

HBsAg -Hepatitis B surface antigen

HCV- Hepatitis C virus

HIV- Human Immunodeficiency Virus

IQR-Interquartile range

KAVI- Kenya AIDS Vaccine Initiative

KENPHIA- Kenya Population-based HIV Impact Assessment

LDL- Lower detection limit.

LIS: Laboratory Information system

LLN- Lower limit of normal

LMIC- Low and Middle-Income Countries

LPV/r-Lopinavir/Ritonavir

mm^3- Cubic millimeter

MTB- Mycobacterium tuberculosis

MTCT- Mother-to-child transmission

NASCOP- National AIDS and STI Control Programme

NDL- Nyumbani Diagnostic Laboratory

NNRTIs-Nonnucleoside Reverse Transcriptase Inhibitors

NRTIs-Nucleoside/ Nucleotide Reverse Transcriptase Inhibitors

NVP- Nevirapine

OIs- Opportunistic Infections

PrEP- Pre-Exposure Prophylaxis

PEP- Post-Exposure Prophylaxis

PI- Protease Inhibitor

PMTCT-Prevention of mother-to-child transmission

PLWH- People living with HIV

RAL- Raltegravir

Rho -Correlation Coefficient

TB -tuberculosis

ULN- Upper limit of normal

WHO- World Health organization

OPERATIONAL DEFINITIONS

Advanced HIV disease (AHD): Someone with a CD4 count below 200

ART: refers to the use of a combination of three or more ARV drugs for treating HIV infection. ART involves lifelong treatment.

ARV: drugs refer to the medicines used to treat HIV.

Elimination; Reduction to zero of the incidence of infection caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent the re-establishment of transmission are required

HIV drug resistance: This is caused by one or more changes (mutations) in the genetic structure of HIV that affect the ability of a specific drug or combination of drugs to block the replication of HIV (*WHO Releases HIV Drug Resistance Report 2021*, n.d.) .

Viral Suppression: refers to a viral load below 1000copies/ mL

Undetectable viral load: refers to viral load below the detection threshold using HIV viral load quantification assays.

Virological failure: This occurs when HIV replication cannot be suppressed
below 1000copies/ mL often despite treatment, and is often defined as a detectable viral load or a significant increase from previously suppressed levels.

Immunological failure: This is a concept involving HIV's impact on the immune system, measured by CD4 cell count. It involves a decline in CD4 cell count below a threshold, indicating immune system damage, or a failure to increase CD4 cell count despite effective HIV treatment.

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

HIV is the agent that causes AIDS (Sharp & Hahn, 2011). While the incidence of HIV has declined globally over the past decade, 1.5 million new cases of HIV infection were reported in 2020,underscoring the continued need for innovative and successful HIV prevention programs (O Murchu et al., 2022). In July 2022, World Health Organisation (WHO) reported that 40.1 million people had died of HIV related causes globally. Currently, approximately 38.4 million People are living with HIV globally and more than two-thirds of these are in the WHO African Region. Notably, 1.7million children aged 0-14 years and 80% are found in Sub-Saharan African nations (Kassa, 2018). In 2022, WHO reported that there were 1.3 million new HIV infections and 130,000 of these were in children <15years (*HIV*, n.d.) . Kenya has approximately 83,000 children aged 0-14 years who are living with HIV and continues to see new infections in children (UNAIDS and AIDSinfo, 2021).

Through various interventions like ART access, routine viral load monitoring, and adherence counselling, HIV is now a manageable health condition. Current treatment guidelines recommend immediate ART initiation upon HIV diagnosis and enhanced adherence support (*Kenya HIV Prevention and Treatment Guidelines, 2022 Edition*, n.d.). This aims to achieve viral suppression that would stop and reverse the damage to the immune system. Although antiretroviral treatment (ART) has reduced AIDS-related deaths, not everyone has access to ART. There are obstacles that can keep certain people from getting timely and effective treatment, including infrastructure, stigma, expense, and restrictions within the healthcare system.access. It has been argued that prevention and awareness programs may prove to be more a viable approach (Govender et al., 2021). In addition to the immediate initiation of ART upon diagnosis, the other global mitigation measures in the health sector to reduce HIV infections and deaths include prevention, diagnosis, and monitoring People living with HIV (PLWH). A regular monitoring of the amount of HIV RNA in the blood has been routinely used in Kenya to determine how well ART is working. It enables timely treatment modifications if necessary and aids in ensuring that the treatment is effective. In addition to enhancing personal health, suppressed viral load also lowers the chance of spreading the infection to others. Such cushioning measures have significantly improved the health of those infected. As such, PLWH are able to suppress viremia and maintain good immunological

profiles without progressing to terminal stages. This includes children who are living with HIV; unlike previously when they had high mortality due to sustained viremia in childhood, they are now able to live into adulthood due to successful ART. Notably, children living with HIV could sustain long-term immunological defects that persist into adulthood despite effective ART. As such, adults who acquired HIV vertically in childhood are likely to differ from those who acquired it horizontally in adulthood. First, they could suffer from the effects associated with the long-term use of ART since they have had lifelong use of the drugs, leading to effects that could differ from those who initiated ART later in life. Secondly, they were exposed to HIV viremia when they still had an immature immune system, probably leading to more severe immune damage. Thirdly, they are likely to have suffered more treatment failure in childhood and adolescence, thus accumulating more immune damage over time. Indeed, pediatric ART failure rates range from 19.3% to over 32.0% (Getawa et al., 2021). Thus, adults who acquired HIV vertically could have poorer immunological and virological profiles when compared to adults who acquired HIV horizontally in adulthood. Yet information on the immunological and virological events that occur in adults who acquired HIV through MTCT is limited, mainly because it is challenging to identify such individuals. While significant progress has been made in preventing MTCT, there are still challenges in managing and improving health outcomes for individuals who acquire HIV through this route.

This study aimed to determine the virological and immunological profiles of adults who acquired HIV vertically in childhood through mother-to-child transmission. This may provide information for designing a targeted clinical management plan. Our study is particularly important in Kenya where these unique adults who are living with HIV since childhood are grouped together with other adults who acquired HIV horizontally due to lack of information on their unique profiles. The information from this study could be used to adjust the Kenya ART guidelines to have tailormade guidelines for this group. Thus, this study is essential in filling this knowledge gap on the long-term impact of HIV MTCT in individuals as they mature into adulthood, to inform their treatment plans.

The study used already generated data in Children of God Relief Institute (COGRI). COGRI is a not-for-profit organization located in Nairobi. It has four programs that operate facilities that serve HIV-infected children and their family members. HIV infected orphans from different parts of the country were registered in childhood in COGRI program as HIV-infected children, and some of these had reached adulthood (>18years) in 2018. Their secondary data on age, HIV viral load, CD4 T cell counts, lymphocytes percentages, neutrophils percentages, monocytes percentages, opportunistic infections (tuberculosis and Cryptococcal meningitis)

and liver function tests to assess the immunological and virological profiles of these adults who are living with HIV was used. Though COGRI has achived such data no comprehensive research done using this data to investigate the health status, immune function, virological profiles and quality of life of these unique

1.2 Problem Statement

The lack of information on adults who acquired HIV through MTCT means we have limited knowledge about their long-term health outcomes. This knowledge gap makes it challenging to provide appropriate medical care and support for this population as they age. To address this problem, comprehensive research is needed to investigate their health status, immune function, virological profiles and quality of life. Filling this knowledge gap will be essential for providing optimal care and support to this often overlooked and vulnerable population.

1.3 Justification of the study

Prevention of mother-to-child transmission (PMTCT) measures is highly effective but not 100%. This is evidenced by the number of cases of MTCT that continue to occur. As such, vertically acquired HIV continues to be a public health problem. The availability of effective ART has ensured that children who acquired HIV vertically in MTCT have a chance to grow into adolescence and adulthood. But adolescents on HIV treatment have lower rates of viral load suppression and adherence compared to adults and children, suggesting that adults who grew up with HIV might have accrued unique profiles over time. Understanding the virological and immunological profiles of individuals who acquired HIV vertically in MTCT and lived through adolescence to adulthood could inform personalized treatment strategies and interventions that are tailored for clinical management of this unique group of adults in Kenya. Yet, this group has remained understudied in the Kenyan setting. This study aimed to address this knowledge gap by using pre-existing data at the COGRI to determine if such adults have different viral load suppression patterns and CD4 T counts, among other immunological biomarkers such as percentages of lymphocytes, neutrophils and monocytes. We also explored possible virological and immunological failure predictors, such as age, liver function tests (Aspartate aminotransferase-AST and Alanine aminotransferase-ALT), and opportunistic infections.

1.4 Research questions

I) What is the prevalence of virological and immunological failure in ART treated adults who acquired HIV through mother-to-child transmission?

II) What are the predictors of virological and immunological failures in ART treated adults who acquired HIV through mother-to-child transmission?

1.5 Research Objectives

1.5.1 Main objective

To determine the virological and immunological profiles of adults who acquired HIV in childhood vertically through MTCT.

1.5.2 Specific Objectives

i. To determine the viral loads of adults who acquired HIV vertically in childhood through MTCT.
ii. To determine the CD4 counts, lymphocytes, neutrophils, and monocytes of adults who acquired HIV vertically in childhood through MTCT.
iii. To determine the predictors of virological and immunological failure in adults who acquired HIV vertically in childhood through MTCT, specifically age, liver function tests (AST and ALT)and opportunistic infections.

1.6 Significance of the study

Studying the outcomes of adults who acquired HIV through MTCT in Kenya is essential for public health, clinical care, and the well-being of affected individuals. It not only helps to raise the standard of living for this group but is also crucial to the larger fight against HIV/AIDS in the nation and worldwide. Specifically, determining the virological and immunological profiles of these adults and their predictors will inform if the treatment guidelines need to be adjusted to optimize the treatment of these individuals.

Identifying virological and immunological profiles is crucial for assessing HIV treatment effectiveness, drug resistance management, resource allocation, and guiding treatment protocols. It helps in early detection of virological failure and drug resistance, allowing for resource allocation and targeted interventions. Virological and immunological data can inform national and international HIV treatment guidelines, leading to cost-effective care and reduced transmission. Successful treatment reduces stigma associated with HIV, leading to better social inclusion and mental health outcomes. Sharing data and best practices can facilitate

international collaboration in HIV research and treatment. The study of virological and immunological profiles can drive innovation in HIV treatment, addressing specific challenges faced by individuals with different profiles.

1.7 Scope of the study

This retrospective cross-sectional study was conducted on secondary data that were collected from adults who were diagnosed with HIV in childhood at COGRI in the year 2018 and stored in the Laboratory Information System. The following data were retrieved: viral loads, CD4 counts, neutrophils, lymphocytes, monocytes, liver function tests, *Mycobacterium tuberculosis* status and Cryptococcal antigen tests.

CHAPTER TWO

LITERATURE REVIEW

2.1 Causative agent

HIV-1 is made up of two copies of positive-sense single-stranded RNA that are noncovalently linked, enclosed in a conical capsid made of the viral protein p24 that is typical of lentiviruses (Deeks et al., 2015). Due to HIV's ability to integrate its DNA into the host genome, the virus is extremely difficult to eradicate using available treatments.

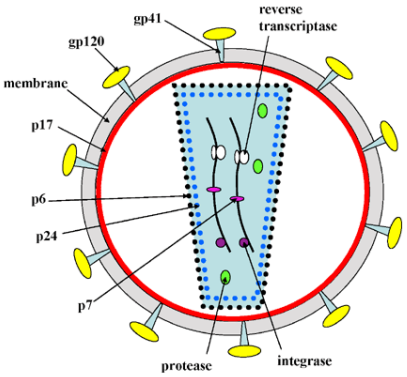

Figure 2. 1 *The structure of HIV particle* **(https://www.aids.gov.hk/pdf/g190htm/01.htm)**

HIV is classified into HIV-1 and HIV-2, both of which originated from the simian immunodeficiency viruses of primates and hence have a zoonotic origin (Sharp & Hahn, 2011). The viruses are transmitted by sexual contact across mucosal surfaces, maternal-infant exposure, maternal-infant exposure, and percutaneous inoculation (Shaw & Hunter, 2012). Studies have shown that people with HIV who keep their viral loads below detection limit pose practically no risk of passing the virus on to others who are HIV-negative through sex, sharing needles, syringes, or other injection equipment, and from mother to child during pregnancy, birth, and breastfeeding. This is because when the viral load is suppressed to undetectable levels, the risk of transmission is drastically reduced. Studies have demonstrated that not every HIV infection develops into AIDS. Antiretroviral therapy (ART) has demonstrated remarkable efficacy in mitigating viral replication, safeguarding the immune system, and halting the advancement of AIDS.

2.2 Pathogenesis

The acute phase begins with flu-like symptoms within the first 3-5 weeks of infection. In this phase of infection, the CD4 T cells are selectively infected by HIV, resulting in high levels of viremia (Dong et al., 2018a) .

Following initial replication in the mucosa upon infection, the virus is transported to the draining lymph nodes. The plasma viremia increases exponentially and peaks at 21-28 days (Dong et al., 2018b) (Omari & Ouifki, 2010). Anti-HIV antibodies are undetectable during the early acute phase; however, seroconversion gradually happens several weeks after infection. After seroconversion, an asymptomatic phase begins due to the spontaneous decline of the peripheral blood viremia, which can last for years (Dong et al., 2018b).

During the asymptomatic phase, HIV continues to weaken the immune system by depleting the CD4 T cells. CD4+ T-cells serve as the central mediators of immune response in humans as they coordinate the adaptive immune responses against infections (Vijayan et al., 2017). HIV, on the other hand, selectively infects CD4 T-cells, destroying them for its own benefit. Cell lysis or syncytia formation occurs once the CD4 T cells are infected with HIV. The infected and uninfected CD4+ T-cells fuse, leading to the spread of the infection (Vijayan et al., 2017) . Without sustainable interventions, this gradually develops into AIDS, the advanced stage of HIV infection (McMichael et al., 2010). AIDS is defined by certain cancers, infections, and other severe long-term manifestations (*WHO Releases HIV Drug Resistance Report 2021*, n.d.). HIV primarily targets CD4 T cells, the virus replicates along with the host cell during normal cellular processes, causing cellular damage and eventually kills the CD4 cells. This leads to a decline in the overall number of CD4 cells in the body, compromising the immune system's ability to respond effectively to infection.

2.3 HIV Lifecycle

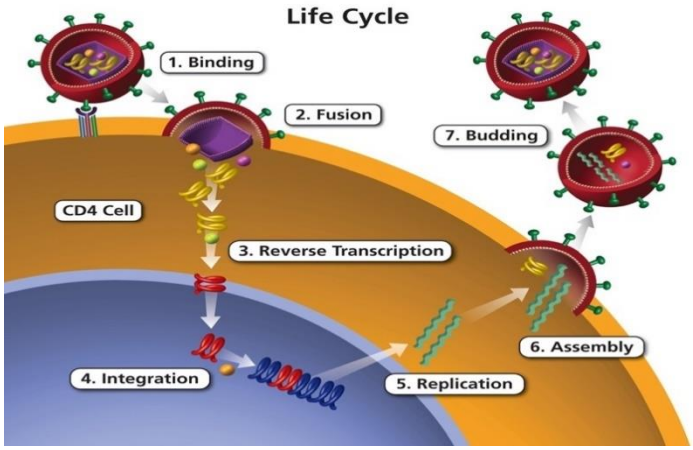

Figure 2. 2 HIV life cycle (OAR - HIVinfo & Info, 2021)

The HIV (human immunodeficiency virus) life cycle is significant when considering virological and immunological failure in the context of mother-to-child transmission (MTCT) of HIV. MTCT occurs when an HIV-infected mother passes the virus to her child during pregnancy, childbirth, or breastfeeding. Understanding the HIV life cycle is crucial in this context because it helps elucidate the factors and mechanisms involved in transmission, treatment, and potential failures.

2.3.1 The HIV life cycle can be divided into:

1. Binding: the HIV attaches itself to molecules on the surface of the CD4 cell, on a CD4 receptor, and then on a CCR5 or CXCR4 co-receptor.
2. Fusion: the HIV viral envelope fuses with the CD4 cell membrane to allow HIV to enter the CD4 cell. The virus then releases HIV RNA and HIV enzymes, such as reverse transcriptase and integrase.
3. Reverse transcription: The reverse transcriptase enzyme converts the RNA genetic material to DNA.
4. Integration: The integrase inserts HIV DNA into the DNA of the host CD4 T cell.
5. Replication: The integrated virus uses the CD4 T cell machinery to make copies of HIV proteins and RNA.
6. Assembly: The proteins and RNA move to the cell's surface and are assembled into non-infectious HIV.

7. Budding: This is the last step in the HIV cycle. HIV buds from the host CD4 T cell and protease is released. Protease breaks up the non-infectious protein chains. Mature infectious HIV is formed when smaller HIV proteins combine (Terms, 2021).

The timing of exposure to the virus during pregnancy, childbirth, or breastfeeding can impact the likelihood of transmission in MTCT. The risk of MTCT is closely linked to the level of HIV in the mother's blood (viral load), maternal immune health, the mother's immune system status and the presence of other sexually transmitted infections (Gouvêa et al., 2020).

In MTCT prevention during pregnancy can be done using antiretroviral therapy (ART) to reduce maternal viral load and prevent transmission to the child. Virological failure can occur if the mother's viral load is not adequately suppressed with ART or if she experiences drug resistance. HIV can enter the uterus through the placental barrier and spread to the tissues of the developing fetus. At this stage, target cells, such as CD4-positive T cells and macrophages, are attached to and fused with. The virus replicates once it has entered the host cell by integrating its genetic material into the DNA of the host cell. Failures at this stage may leave the mother's bloodstream without viral suppression, increasing the chance of transmission to the fetus.

Breast milk contains both HIV and protective immune factors. The balance between these factors can influence the risk of MTCT during breastfeeding. Viral particles are assembled and discharged from infected cells throughout the stages of assembly and budding. Failures at this stage enhance the chance of transmission during breastfeeding by increasing the viral load in the mother's breast milk. Understanding this interaction is essential in designing strategies to minimize immunological failure.Immunological failure in MTCT can lead to infant's incapacity to fend against HIV infection as a result of a weakened immunological response making it more susceptible to HIV because of their underdeveloped immune system, which is not fully effective. Some newborns may inherit HIV-specific antibodies from their mothers, which may offer momentary protection. Over time, these defenses weaken, making the child more prone to illness. As a child's immune system matures, it might be unable to successfully fight off the virus, potentially resulting in immunological failure. Breast milk both contains HIV and immune-protective substances. The ratio of these factors can significantly influence the risk of MTCT during breastfeeding.

In summary, the HIV life cycle plays a significant role in understanding and addressing virological and immunological failure in mother-to-child transmission of HIV. Preventing these failures involves a multifaceted approach that encompasses maternal treatment, infant protection, and a deep understanding of the virus's lifecycle in both the mother and child.

Addressing these issues could lead to reduction in the transmission of HIV from mother to child and improve the overall health outcomes for both.

There are various individual differences in the prognosis for HIV. While some people may experience a faster rate of disease progression, others may experience a slower rate. This natural path can be dramatically changed by the introduction of antiretroviral medication (ART), which inhibits viral replication, protects CD4 T cells, and enhances general health of the mother and child.

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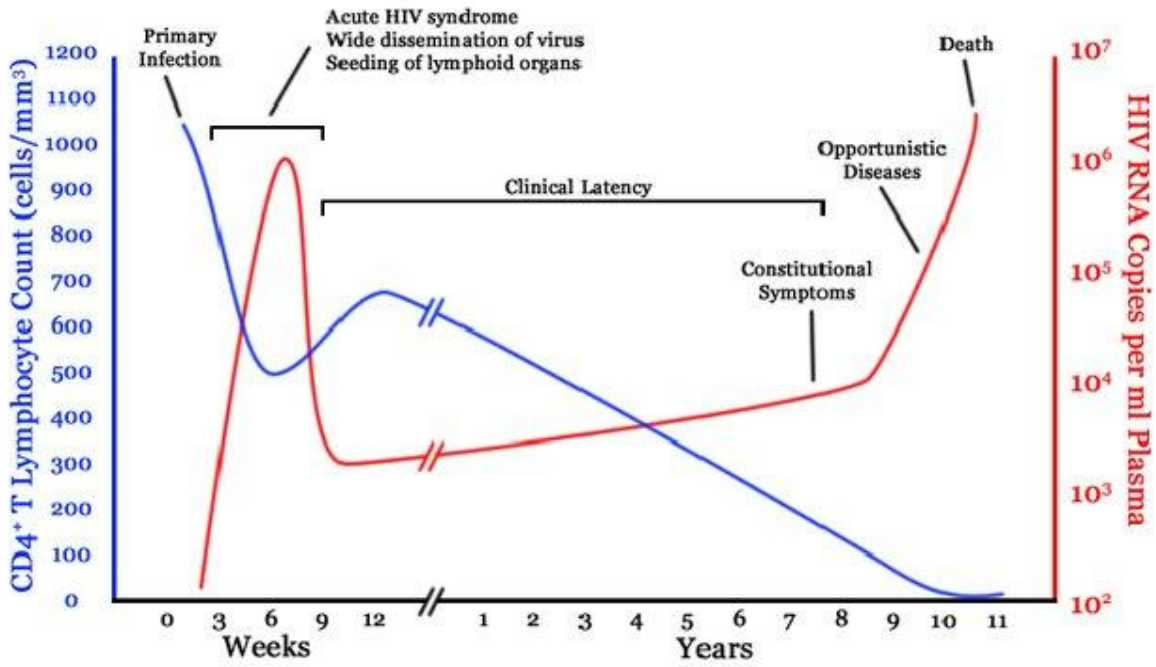


Figure 2. 3 A graph of the relationship between HIV viral load and CD4 T cells counts over the average course of untreated HIV infection any particular individual's disease course may vary considerably (Omari & Ouifki, 2010).

2.4 Antiretroviral drugs

Antiretroviral drugs are medications that are used to prevent a retrovirus, such as HIV, from replicating (Terms, 2021). The various stages of the retroviral life cycle, including viral entry, reverse transcription, integration, and assembly, are inhibited by antiretroviral medications (McKinney, 2006) . These drugs have significantly improved the prognosis and quality of life of people living with HIV/AIDS. Studies indicate that the recovery of peripheral CD4+ T-cells occur following ART suppression of viremia in most patients (Zhang et al., 2015). Major

classes of antiretroviral drugs include; Non-Nucleoside Reverse Transcriptase Inhibitors, Nucleoside Reverse Transcriptase Inhibitors, Protease Inhibitors, Fusion inhibitors, Entry inhibitors and Integrase transfer.

Table 2. 1 Classes of antiretroviral drugs

Class Of Drug	**Example Of Drugs**	**Mechanism of Action**
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIS)	Efavirenz	Allosteric inhibition of RNA- and DNA-dependent DNA polymerase activity.
Nucleoside Reverse Transcriptase Inhibitors (NRTIS)	TDF, ABC, 3TC, FTC, AZT	Act by competitive inhibition of HIV-1 reverse transcriptase.
Protease Inhibitors (PIs)	Atazanavir, Indinavir, **LPV/r**	Inhibit protease enzyme used by HIV to cleave nascent proteins for the final assembly of new virions.
Fusion Inhibitors	Enfuvirtide	Inhibit HIV from binding to human immune cells
Entry Inhibitors	Maraviroc	Inhibits HIV from entering human immune cells
Integrase strand transfer inhibitors (InSTIs)	**Dolutegravir, Raltegravir**	**act by binding to the enzyme integrase**

Table 2. 2 Preferred ART Regimen for infants, children, adolescents, and adults

(Kenya HIV Prevention and Treatment Guidelines, 2022 Edition, n.d.)

Weight/ scenario	**First-line ART**	**Second-line ART**		**Possible 3rd Line Regimen**
< 30 kg	ABC (or AZT) + 3TC + DTG	DRT-based second-line2		
	ABC + 3TC + LPV/r	Take a sample for DRT and change to AZT +3TC + DTG while awaiting DRT results; modify based on DRT results if indicated	**Children**	DTG + 3TC + DRV/r DTG + AZT + 3TC + DRV/r DTG + ABC (or TDF) + 3TC + DRV/r ETV + 3TC + DRV/r
	AZT + 3TC + LPV/r	Take a sample for DRT and change to ABC + 3TC + DTG while awaiting DRT results; modify based on DRT results if indicated	**Adults**	DTG + 3TC + DRV/r DTG + AZT + 3TC + DRV/r DTG + TDF + 3TC + DRV/r DTG + TDF (or AZT) + 3TC ETV + 3TC + DRV/r
	ABC + 3TC + EFV	AZT + 3TC + DTG		
	AZT + 3TC + EFV	ABC + 3TC + DTG		
≥ 30 kg or ≥ 15 years old	TDF (or ABC) + 3TC + DTG (or PI/r)	DRT-based second-line2		
	TDF (or ABC) + 3TC + EFV	TDF + 3TC + DTG		
	AZT + 3TC + EFV	TDF + 3TC + DTG		

2.5 ART Treatment and drug resistance

WHO guidelines, Kenyan national guidelines, and several studies recommend immediate initiation of the ART upon HIV diagnosis (or at least within two weeks) regardless of the CD4 T cell counts, age, pregnancy status, or co-morbidities, except in cases of TB meningitis or Cryptococcal meningitis (*Kenya HIV Prevention and Treatment Guidelines, 2022 Edition*, n.d.). Antiretroviral therapy works by suppressing HIV replication, leading to undetectable copies of HIV in plasma below the current assays' limit of detection, subsequently leading to improved survival of PLWH and reduced risk of HIV transmission (Arts & Hazuda, 2012). To retain the viral load at undetectable levels, measures like adherence monitoring, counselling support, and HIV viral load monitoring have been emphasized as support for PLWH. The emergence of drug-resistance mutations that may compromise treatment options is associated with poor adherence or intermittent access to ART, resulting into treatment failure (*WHO Releases HIV Drug Resistance Report 2021*, n.d.) . Understanding and managing HIV's virological and immunological aspects, addressing drug resistance, and ensuring regular monitoring, treatment adherence, and ongoing research are crucial for improving long-term health outcomes.

2.6 Virological and Immunological Profiles in ART Treatment

The goal of ART is to suppress viral replication to reduce the patient's viral load to undetectable levels. Undetectable viral load reduces the risk of disease progression and HIV transmission to HIV-negative partners (Larmarange et al., 2018).

Studies have indicated that HIV infection itself, as well as some antiretroviral drugs, can harm various organ systems causing hepatic and renal diseases, neurological defects, osteoporosis, metabolic complications like diabetes mellitus and dyslipidaemia (Goldschmidt & Chu, 2021) Between 14% and 20% of HIV-positive people on ART have elevated liver transaminases (Qin et al., 2019). Elevation of liver transaminases could lead to liver damage or failure if not monitored closely. Studies have also indicated that HIV-infected individuals experience anemia, neutropenia, and thrombocytopenia (De Santis et al., 2011)

Therefore, individuals living with HIV require comprehensive medical care that addresses the virus and associated comorbidities to ensure optimal health outcomes. Regular monitoring and managing these conditions are crucial for maintaining a good quality of life for people with HIV. It is also noted that substandard adherence and drug intolerance contribute to virologic

failure and regimen discontinuation in patient cohorts from earlier era of combination ART (hiv.gov, 2023).

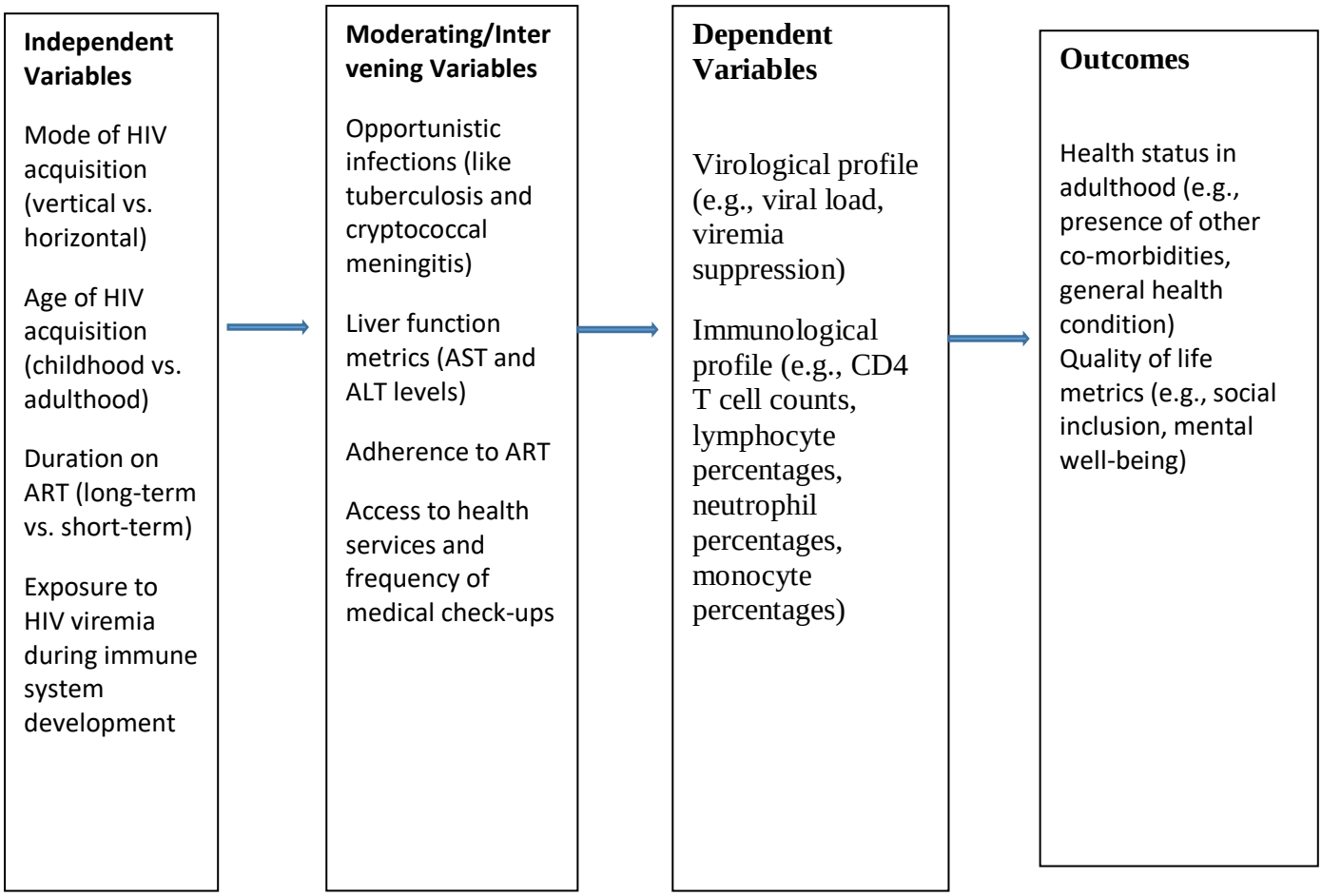
Significant treatment failure among HIV-infected children is associated with having co-infections, being on ART for an extended period, regimen change, and being male. Therefore, timely identification and monitoring of ART failure is necessary to enhance the benefit and to prevent further complications (Getawa et al., 2021). Therefore, managing HIV in children and adolescents involves a comprehensive approach that considers both virological and immunological profiles.

2.7 HIV in Children and Adolescents

The prevalence of virological treatment failure among children and adolescents living with HIV on ART remains high (Bitwale et al., 2021). Children and adolescents are important populations that face challenges in viral suppression, clinical and ART adherence.

Available studies indicate that the prevalence of HIVDR in young people with perinatal HIV and children living with HIV is typically high in both resource-rich and resource-limited settings, most likely as a result of a combination of prolonged ART exposure and ART adherence challenges (Li et al., n.d.). This group of children and young people grow into adulthood with these challenges and may benefit more from different service delivery models that are tailored to their needs. Considerations like age, developmental stage, and social support should be considered as these models are designed to meet the particular needs of these populations. In settings with limited resources, there is a lack of readily available information on viral suppression in HIV-positive children and adolescents receiving ART. Studies show a suppression rate well below 75%, below the virologic suppression set out in the 90–90–90 World Health Organization target (Onyango et al., 2023).To maintain viral suppression, efficient access to HIV drugs and adherence to the prescribed regimen is key. High viremia is associated with increased risk of HIV-1 vertical transmission which can be reduced to <1% upon implementing appropriate measures like cesarean section, use of ART by HIV-1-infected mothers during pregnancy and the neonatal ART administration, and bottle-feeding and adhered to after birth (Yu et al., 2021).

2.8 Conceptual Framework



The mode of HIV acquisition, age of HIV acquisition, duration on ART, and exposure to HIV viremia during immune system development, are all interrelated factors that, taken together, affect the virological and immunological outcomes in people living with HIV. To customize HIV care and treatment and improve each patient's health outcomes, it is essential to comprehend these characteristics. Access to healthcare services, adherence to antiretroviral therapy (ART), opportunistic infections, and measures of liver function can all act as moderating or intervening factors in the association between HIV infection and virological and immunological outcomes. Their influence on virological and immunological responses emphasizes the significance of all-encompassing care and monitoring in effectively controlling HIV.

The study made use of major virological and immunological characteristics that are essential for determining the efficacy of HIV treatment, tracking the development of the disease, and

making educated decisions regarding the care and treatment of HIV-positive people. These are crucial parameters that provide information about the efficacy of interventions, and enhancing health and quality of life as a key objective in HIV care and management.

CHAPTER THREE

METHODOLOGY

3.1 Design of the Research

This was a retrospective descriptive study design conducted at Children of God Relief Institute (COGRI) on pre-existing data from ART-treated adults diagnosed with HIV in childhood. Laboratory biomarkers used in monitoring HIV among ART- experienced patients at COGRI were used in descriptive analyses, namely viral loads, CD4 T cell counts, Lymphocytes, neutrophils and monocytes. Associations with possible predictors of virological and immunological failure, such as liver function tests (AST, ALT) and opportunistic infections, were also investigated.

3.2 Study area

This study was carried out within the Children of God Relief Institute (COGRI), a not-for-profit organization. It serves four programs: Nyumbani Childrens Home, Nyumbani Diagnostic Laboratory (NDL), Lea Toto Community outreach Program, and Nyumbani Village. Nyumbani Children's Home was founded in 1992 to provide life-saving care and a loving home to mostly abandoned children created by the AIDS pandemic in Kenya. The children live at the Children's Home until they are healthy and self-reliant. The Nyumbani Diagnostic Laboratory (NDL) was established in 1998 and this would later help in monitoring HIV through CD4 T cell counts, viral load and other tests. The NDL was ISO accredited by KENAS in 2013. The Lab serves the COGRI programs and it serves as a referral for other Health facilities and walk-in clients. The Lea toto Community outreach program has facilities located in the slum areas. It is a HIV/AIDS community outreach program that operates facilities that serve HIV-positive children and their family members. Nyumbani Village is a project that hosts children and grandparents displaced by the Kenya AIDS epidemic where they live together in small cottage units as blended families. The core business of COGRI is the Provision of comprehensive care and support to HIV-infected and affected children and their families. That covers medical, psycho-social, spiritual, moral, nutritional, educational services, and parental care.

This study analyzed data obtained from the laboratory tests done on patients registered at COGRI Program. These data are stored in an access- controlled Laboratory information system.

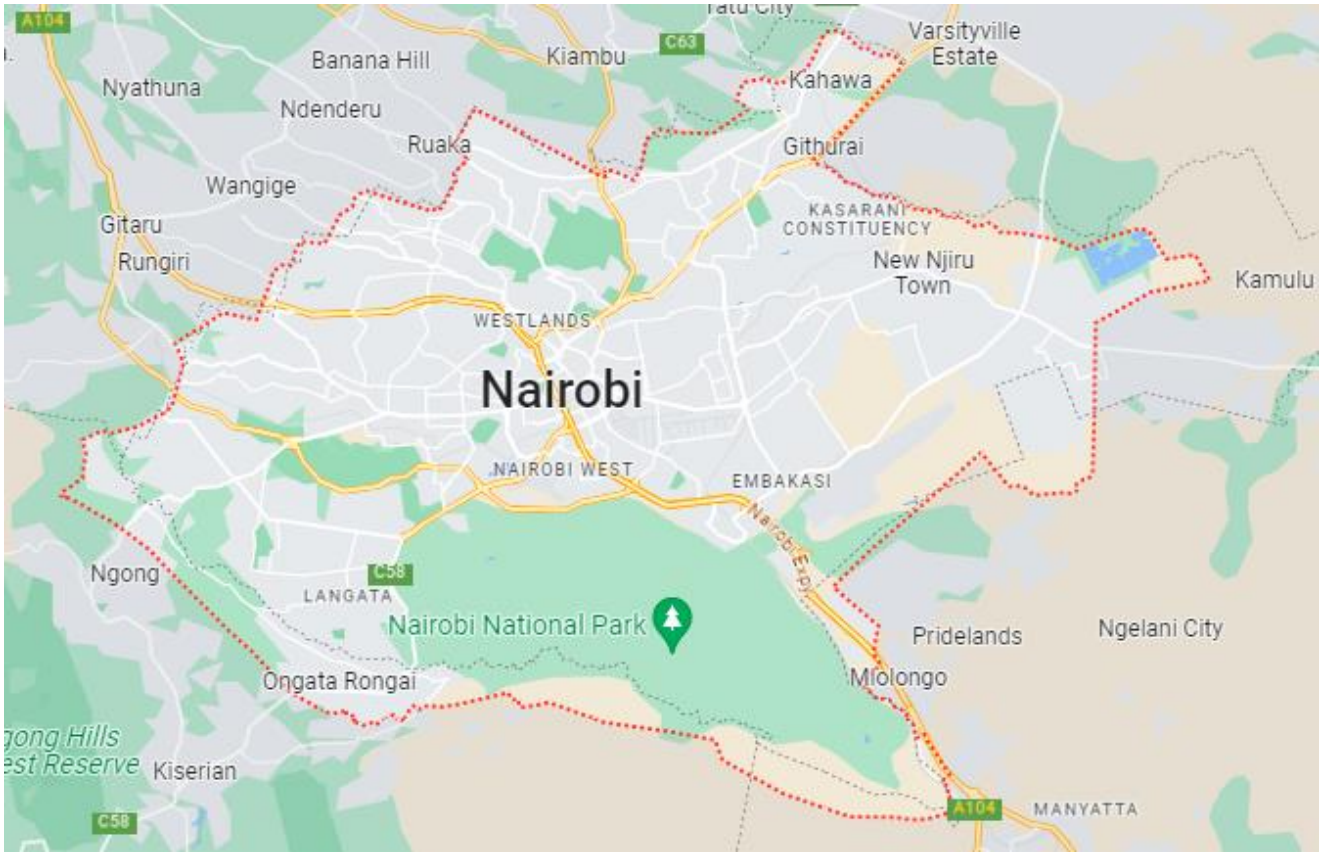


Figure 3. 1 A map of Nairobi County Where the study was conducted

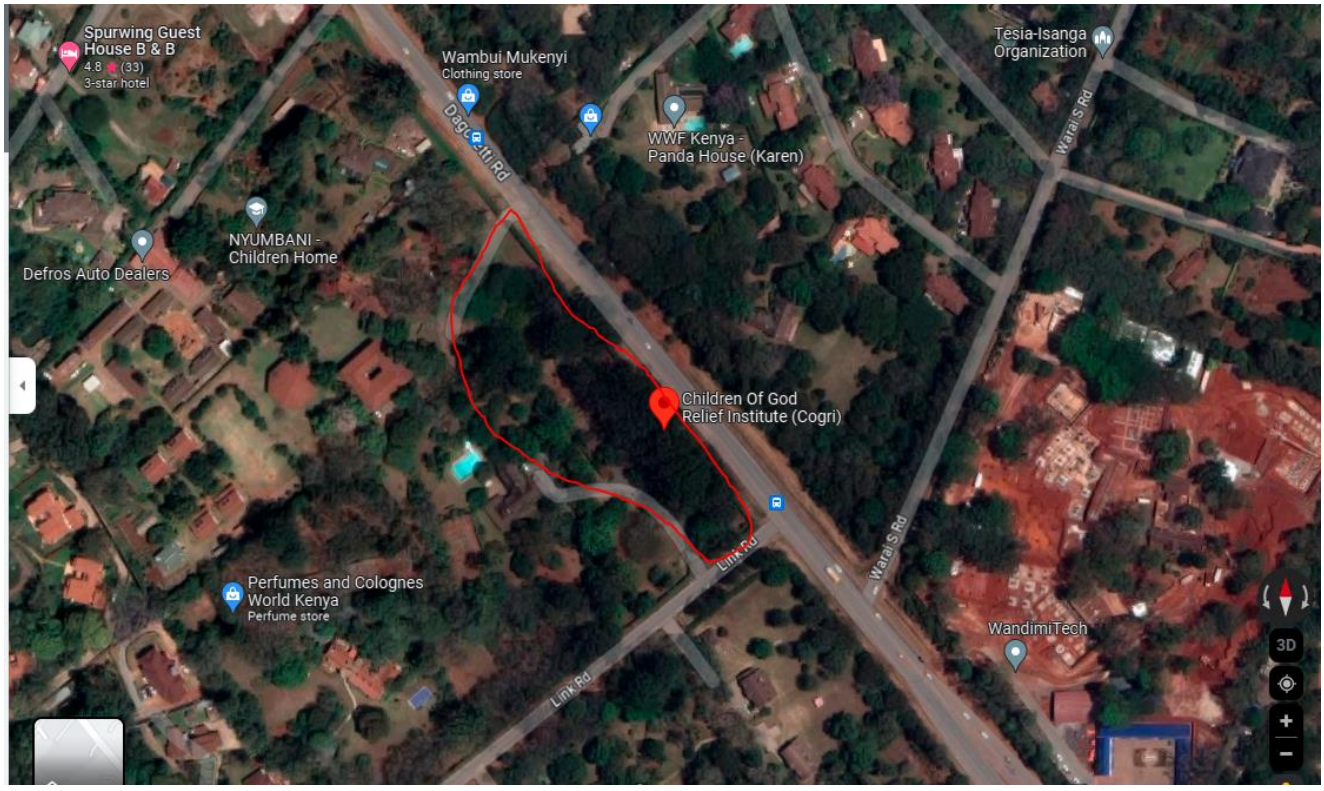


Figure 3. 2 A Map of the Study area

3.3 Study population

The study population included the ART-treated adult population registered in COGRI. Socio-demographic and clinical variables such as age, opportunistic infections and laboratory biomarkers were collected and compiled in an excel.

3.4 Inclusion criteria

- Individuals who were adults in 2018 (18 years and above) but were registered in the COGRI program in childhood as HIV-infected children.
- Individuals with at least one of the following laboratory biomarkers data; CD4 T cell counts, viral load, lymphocytes, monocytes neutrophils, AST and ALT.

3.5 Exclusion Criteria

- Individuals lacking data on laboratory biomarkers.
- Individuals who were registered in the COGRI program in adulthood.

3.6 Sample size determination and formula

Initial sample size calculations using the "power one proportion" function in Stata IC version 15.1 had indicated that we needed 86 participants. This was based on the assumption that 90% of HIV-infected ART treated adults have controlled viral loads based on the KENPHIA 2018 Preliminary report ((*KENPHIA 2018 PREL REP Fin_alt2_USAID.Indd 1*, n.d.). That sample size would have enabled detection of a 10% difference (80% viral loads suppression rates) in ART-treated individuals who acquired HIV vertically with a power of 80%, a probability of type I error of 0.05 and a probability of type II error of 0.2.

However, since this was a retrospective study utilizing archived data and additional collections of information from the participants were not needed, all available data from individuals who met the inclusion criteria and were registered in COGRI Program as HIV infected children in childhood and were above 18 years of age in year 2018 were used to maximize the power of the study. These were 660 eligible participants.

3.7 Data Collection Procedures and Data Collection Tools

The study used information from thorough review of the NDL Lab Information System and when needed NASCOP dashboard. Abstraction of data of all the eligible participants registered under COGRI facilities was obtained for the year 2018. After log in to the Laboratory information system, a tab of all lab reports is displayed in the menu bar. January 1st to

December 31st 2018 was selected to filter all the available data sets. This was uploaded automatically in to an excel format. Participants without the study immunological and or virological profiles were excluded.

Nyumbani lab has credentials into NASCOP system and for data abstraction, a search button for the specific participant was used, the unique comprehensive care centre (CCC) number was entered then search button. This displayed specific information that could be missing in the LIS.

In instances where a participant had more than one immunological or virological profile measurement in 2018, an average of the lab results within the year was calculated. This information was documented on a Microsoft excel and analyzed using Stata software. A summary of the characteristics of the study participant's descriptive statistics was done.

3.8 Sources of Data

The patient's information was archived in the Laboratory information system in NDL. The LIS captures the date, patient's identification, Age, unique CCC number, tests, and the lab results.

3.9 Variables

Dependent Variables

1. HIV Viral load
2. CD4 Absolute Counts
3. LFTs (AST, ALT)
4. Lymphocytes counts
5. Neutrophils counts
6. Monocytes counts
7. Opportunistic infections

Independent variable: Age

3.10 Data Management

After identifying individuals that met the inclusion criteria, the data were cleaned then coding was done to protect clients' information. Quality control of the collected data was done by manually cross-checking the data to ensure the correctness and reliability. The data were stored in password-controlled computers by principal investigator and the supervisors.

3.11 Analysis of Data

Data were analyzed using Microsoft Excel and Stata software. Proportions of individuals with viremia or suboptimal immune parameters were determined. Associations between profiles in adulthood and their predictors (age and liver function tests) were analyzed.

Data was imported from an excel file that was abstracted from the Lab information system into Stata's data editor. Data exploration was done to summarize data using descriptive statistics (median, mean)and graphs. A command-driven syntax was used to enter commands in the Stata command window to execute the analyses. The output of the command included summary statistics and a p-value associated with the statistical test. p-value less than the significance level of 0.05 was considered statistically significant.

Data was analyzed and presented by constructing tables and graphs of medians and quantiles. Summaries of the proportions of study participants who met various criteria were presented in tables.

3.12 Ethical Considerations

COGRI Executive Director approved retrieval of data from the Laboratory records. The study was also reviewed and approved by Kenyatta National Hospital (KNH) and the University of Nairobi (UoN) Ethics and Research Committee (KNH-UoN) (approval number P76/01/2023). The study was also approved by the National Commission for Science, Technology and Innovation (NACOSTI) (License No: NACOSTI/P/23/28697). The study used secondary data from the LIS hence waived consent since it poses minimal risk to participants. To maintain confidentiality of study participants, names and other personal identifiers were delinked from the working dataset. Data access control procedures were adhered to as stipulated in Laboratory confidentiality procedure. There was restricted access to the dataset to only authorized individuals, the principal investigator, the IT administrator and the supervisors. The data was stored in a secure environment with controlled access example password-protected databases encrypted excel storage.

3.13 Study limitations and Minimization

Using historical LIS data may introduce biases or inaccuracies, especially if the data was not originally collected for research purposes. This could affect the reliability of the results.. To ensure data accuracy and reliability, we mitigated this by implementing crosschecking methods, the study had also clearly articulated research objectives and data collection methods

aligned with these objectives. A standard procedure for data collection was used to minimize variations and biases.

Examination of data for internal consistency and logical relationships between variables was done and there were periodic verification that data values were within the expected ranges this helped to timely identify errors. We implemented data cleaning procedures to correct errors, missing values, or inconsistencies in the dataset.

Use of historical data wasclearly acknowledged in the study's conclusions due to possibilities of selection bias because the data used was not collected for the purpose of this study. The characteristics of the selected sample may not be representative of the broader population or may not generalize well to the current context.
This historical datasets lacked certain variables like the opportunistic infections which were crucial for the research questions. Not all participants had complete variables and this limited the ability to explore certain relationships to conduct comprehensive analyses.

This secondary data suffered from survivorship bias, since we only included data of individuals that were still in COGRI leaving out those who had exited before 2018We also lacked a comparator group of ART-treated adults who acquired HIV horizontally in adulthood. To mitigate this, we referenced data that were collected in a country-wide survey in the same year for comparisons.

CHAPTER FOUR

RESULTS

4.1 Characteristics of study participants

For this retrospective descriptive study, the specific objectives of this study were to determine the viral loads, CD4 T cell counts, AST, ALT, lymphocytes, neutrophils and monocytes of ART-treated adults who acquired HIV vertically in childhood through MTCT. The study also aimed to determine the associations between virological and immunological failure and other covariates, such as age and opportunistic infections.

Six hundred and sixty HIV-positive adults who were registered in COGRI programs in childhood as HIV infected children were studied. They comprised of 50.1% (331) males and 49.8% (329) females. Ages ranged from 18 to 26 years. All participants were on ART. 90% (595) were on the first line ART while 1.7% (11) was on second line ART and the rest did not have data on the specific ART regimen. The participants had laboratory results available as follows: HIV viral load n=652, CD4 T cell counts n=469, AST & ALT n=301, neutrophils, lymphocytes, monocytes n=370, *Mycobacterium tuberculosis* (MTB) n=6 and Cryptococcal antigen (CrAg) n=13 (Figure 4.1).

The descriptive statistics on the variables were reported as proportions, medians, and interquartile ranges.

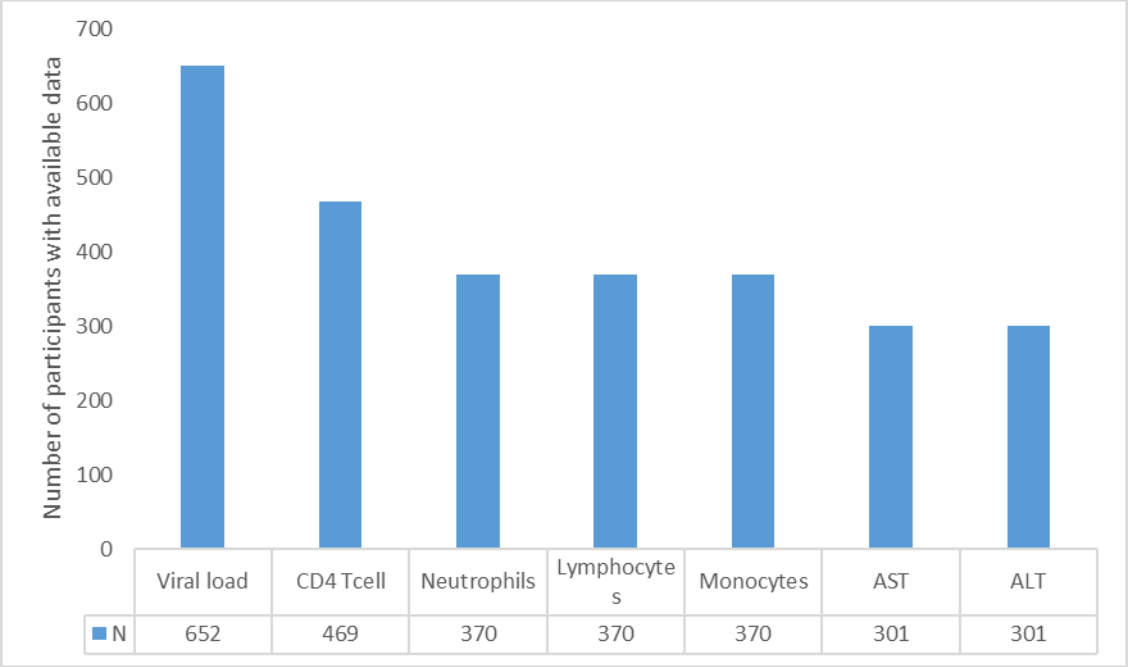


Figure 4. 1 Data availability for various biomarkers that were assessed in the study

Information on HIV viral load, an important virological indicator, for the study's 652 participants. Immunological status of 469 participants is provided by their CD4 T cell counts. Data on liver function, include AST and ALT values, were gathered for 301 people. For 370 participants, counts of neutrophils, lymphocytes, and monocytes were included to shed light on the participants' immune cell makeup. Information on Mycobacterium tuberculosis, a probable co-infection with tuberculosis, for 6 participants. 13 participants' data on their cryptococcal antigens are presented, indicating the potential for screening for cryptococcal infections.

4.2 HIV viral loads

From 660 ART-treated participants, 652 patients had results for HIV viral load. 64% (415) of the participants had undetectable HIV-1 viral RNA level (<50 copies/mL). 73% (479) of the participants had suppressed viral load below 1000 copies/mL (Table 4.1). Notably, a national survey in the general population reported that 90.6% of ART-treated adults had viral suppression (below 1000 copies/mL) in the same year, suggesting that adults who acquire HIV through MTCT in this study have higher rates of virological failure when compared to those who acquired HIV horizontally in adulthood (*KENPHIA 2018 PREL REP Fin_alt2_USAID.Indd 1*, n.d.)

4.3 CD4 T cell count

Of the 467 participants that had their CD4 T cell counts within the period and out of these, 59 (13%) had CD4 T cell count of <250 cells/mm^3. The cohort's median CD4 T cell count was 569 cells/mm^3. The minimum and maximum CD4 T cells were 4 and 1919 cells/ mm^3, respectively. It was noted that 17 participants had CD4 T cells <250 cells/ mm3 even though they had suppressed viral loads (<1000 copies/mL) (Table 4.1).

4.4 Neutrophils, Lymphocytes and Monocytes

370 participants had data on percentages of neutrophils, lymphocytes, and monocytes with a median of 45%, 45%, and 5.5%, respectively. 54 participants (15%) had neutropenia (<35% neutrophils) and 8 participants (2.2%) had neutrophilia (>75% neutrophils). 12 participants (3.2%) had lymphopenia (<20% lymphocytes) and 124 participants (34%) had lymphocytosis (>50% lymphocytes). 2 participants (0.5%) had monocytopenia (<2% monocytes) and 9 participants (2.43%) had monocytosis (>12% monocytes) (Table 4.1).

4.5 Liver Transaminases; AST and ALT

301 participants had their AST and ALT tested with a median of 24.45 IU/L and 17.6 IU/L, respectively. The minimum and maximum of ALT were 7 and 135.5 respectively while AST had minimum and maximum of 12.4 and 608.8 respectively. The assay upper limit of Normal (ULN) was ALT 42 IU/L and AST 37 IU/L. A total of 31 participants had AST >=37 IU/L, 2 with >3*ULN and 1 had > 5*ULN. 15 participants had ALT >=42 IU/L and 1 participant had 3*ULN (Table 4.1).

Table 4. 1 Distribution of participants (proportions) within various virological, immunological and liver function variables

Variable		% (N)
Viral load	Undetectable (<50 copies/ml)	64% (415/652)
	Suppressed (<1000 copies/ml)	73% (479/652)
CD4	<250 cells/uL	13% (59/(467)
Neutrophils	Neutropenia (<35%)	15% (54/370)
	Neutrophilia (>75%)	2.2% (8/370)
Lymphocytes	Lymphocytopenia (<20%)	3.2% (12/370)
	Lymphocytosis (>50%)	34% (124/370)
Monocytes	Monocytopenia (<2%)	0.5% (2/370)
	Monocytosis (>12%)	2.4% (9/370)
AST1	>=37 IU/L	10.3% (31/301)
ALT	>=42 IU/L	5% (15/301)

4.6 Associations between viral loads and CD4 T cells counts, percentages of neutrophils, percentages of lymphocytes, percentages of monocytes and liver function tests

To determine if having detectable viral loads was associated with different immunological and liver function profiles, the participants were first grouped into those with undetectable viral loads (<50 copies/mL) and those with detectable viral loads (>/=50 copies/mL). CD4 T cells counts, percentages of neutrophils, percentages of lymphocytes, percentages of monocytes and liver function tests were then compared between the 2 groups. The group that had detectable viral loads (>/=50 copies/mL) also had lower CD4 T cells counts (P<0.001), lower percentages of lymphocytes (P=0.036) and higher percentages of monocytes (P<0.001) when compared to the group that had undetectable viral loads (<50 copies/mL). There were no differences in age, percentages of neutrophils and liver function tests between the 2 groups (Table 4.2 and figure 4.2). The p-value of less than 0.001 indicates statistical significance between detectable viral loads and lower CD4 T cell counts. This finding imply that maintaining undetectable viral loads with antiretroviral therapy (ART) is linked to increased CD4 T cell counts, which are normally positive indicators of a healthier immune system. This discovery may influence HIV treatment plans by highlighting the significance of regular ART compliance in achieving and

maintaining undetectable viral loads. It also emphasize the advantages of starting antiretroviral therapy (ART) early to optimize CD4 T cell numbers and immune system performance.

Individuals with detectable viral loads (50 copies/mL or higher) were linked to higher percentages of monocytes.This finding may have implications for understanding the impact of detectable viral loads on the immune system. Highlighting the need for targeted interventions to manage immune activation or inflammation in individuals with detectable viral loads .

Table 4. 2 Comparisons of CD4 Tcells count, neutrophils, lymphocytes, monocytes, AST, and ALT between groups with undetectable and detectable HIV viral load (>=50 and <50 copies/mL)

	Detectable (>=50) Median (IQR)	Non-detectable (<50) Median (IQR)	Total Median (IQR)	p-value
Age (years)	20 (18-21)	20 (18-21)	20 (18-21)	0.61
CD4	383 (225-556)	651 (487.5-831.5)	569 (377.5-753)	<0.001
Neut	46 (38.5-55)	45 (37.5-53)	45 (38-54)	0.21
Lymp	44 (37-50.5)	46 (39-53)	45 (38-52)	0.036
Mon	6 (4-8)	5 (4-7)	5.5 (4-7)	<0.001
AST	24.55 (20.1-29.1)	24.45 (20.3-30)	24.45 (20.25-29.65)	0.95
ALT	16.85 (13.6-22.4)	18.2 (13.9-24.1)	17.6 (13.8-23.4)	0.063

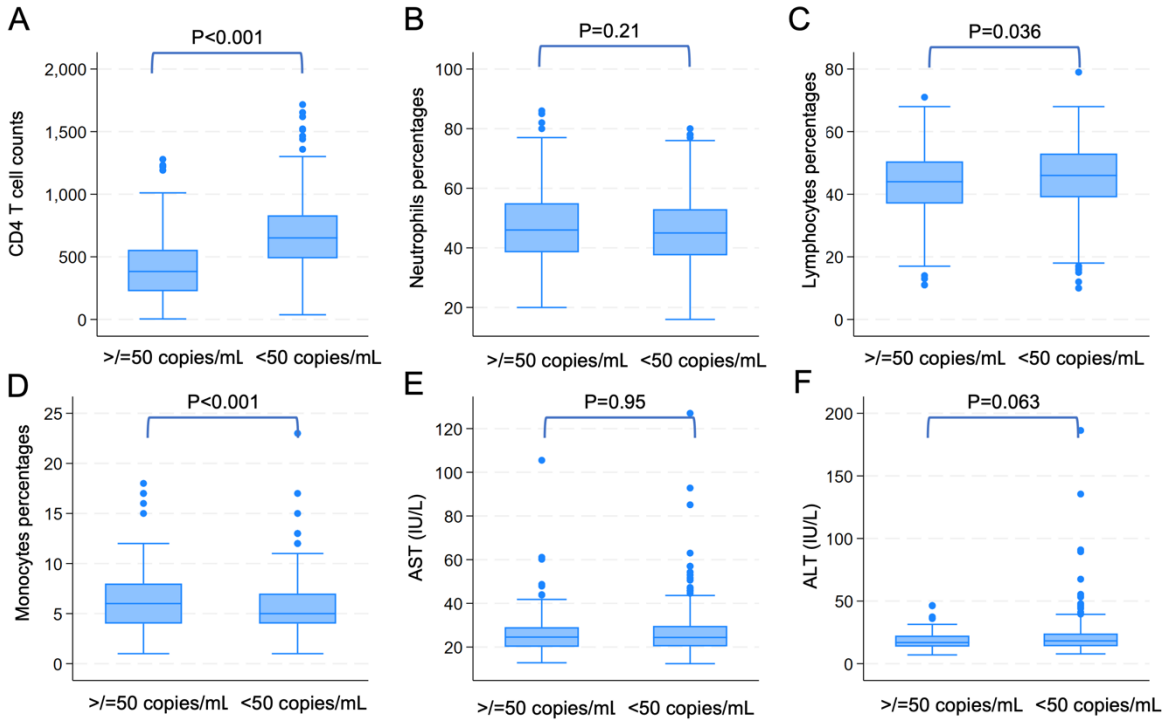


Figure 4. 2 Comparisons of CD4 T cells count, neutrophils, lymphocytes, monocytes, AST, and ALT between groups with undetectable and detectable HIV viral loads.

To further determine if having virological failure was associated with different immunological profiles, the participants were then grouped into those without virological failure (<1000 copies/mL) and those with virological failure (>/=1000 copies/mL). Similar to the group that had detectable viral loads, the group that had virological failure (>/=1000 copies/mL) also had lower CD4 T cells counts (P<0.001), lower percentages of lymphocytes (P=0.024) and higher percentages of monocytes (P<0.001) when compared to the group that did not have virological failure (<1000 copies/mL). Notable, the group without virological failure also had higher ALT values. There were no differences in age and percentages of neutrophils between the 2 groups (Table 4.3 and figure 4.3

Table 4. 3 Comparisons of CD4 Tcells count, neutrophils, lymphocytes, monocytes, AST, and ALT between groups with and without virological failure (>=1000 and <1000 copies/mL)

	Virological failure (>=1000) Median (IQR)	No virological failure (<1000) Median (IQR)	Total Median (IQR)	p-value
Age (years)	19.5 (18-21)	20 (18-21)	20 (18-21)	0.52
CD4	349 (182-502)	646 (475-811)	569 (377.5-753)	<0.001
Neut	46 (38-55)	45 (38-53)	45 (38-54)	0.3
Lymp	43 (36-51)	46 (39-53)	45 (38-52)	0.024
Mon	6 (4-8)	5 (4-7)	5.5 (4-7)	<0.001
AST	24 (19.7-28.6)	24.6 (20.3-30.3)	24.45 (20.25-29.65)	0.39
ALT	16.6 (13.3-20.9)	18.3 (14.1-24.1)	17.6 (13.8-23.4)	0.022

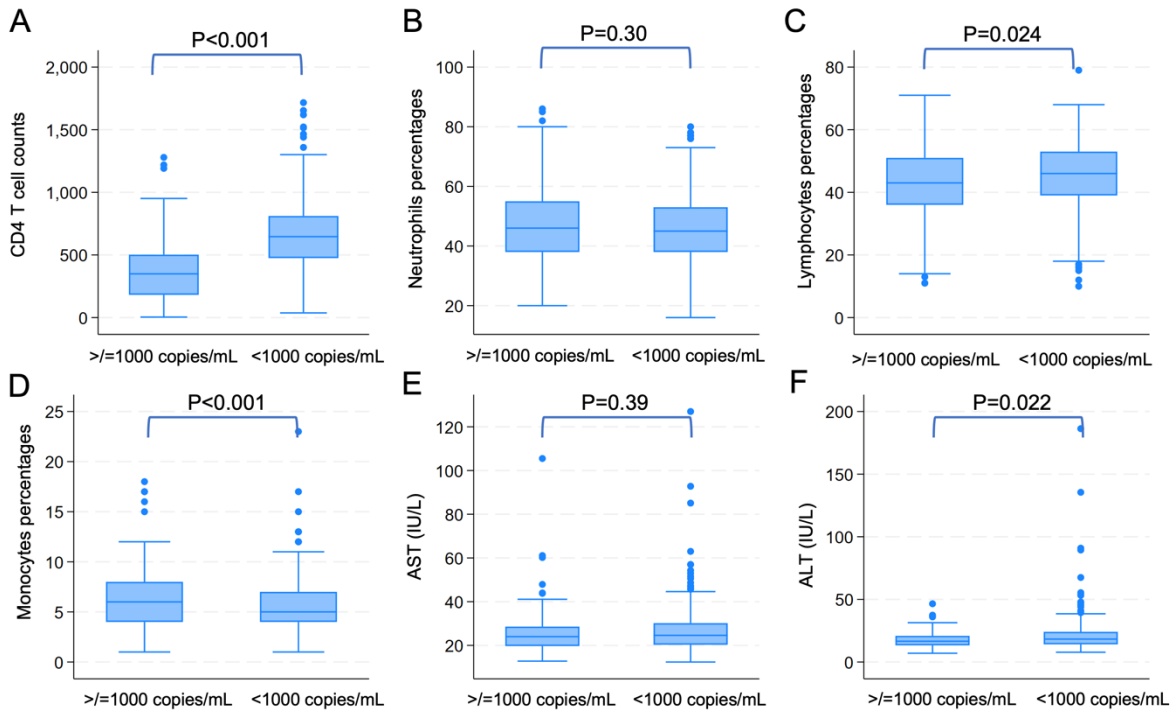


Figure 4. 3 Comparisons of CD4 Tcells count, neutrophils, lymphocytes, monocytes, AST, and ALT between groups with and without virological failure

4.7 Opportunistic infections

Tuberculosis and Cryptococcus meningitis are opportunistic infections that frequently affect people with weakened immune systems, especially those with advanced HIV/AIDS. These infections can have serious consequences and must be identified and treated immediately. HIV impairs immunological function, increasing a person's susceptibility to TB infection, and TB can hasten the course of HIV. Cryptococcus meningitis infects the brain and spinal cord, usually in patients with weakened immune systems, such as those with severe HIV/AIDS.

The Kenya ART guidelines indicate that these two diseases should be routinely monitored in people with low CD4 T cells. In this study, 21 participants had CD4 count of less than 100 cells/cumm. 13 of them had been tested for Cryptococcus meningitis and 1 had a positive result. On the other hand, 6 individuals had been tested for Mycobacterium tuberculosis across the cohort regardless of CD4 counts, with one having a positive MTB result with rifampicin resistance.

CHAPTER FIVE

DISCUSSION CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion of the Results

5.1.1 Virological profiles in ART-treated adults who acquired HIV through MTCT

Due to limited resources and knowledge, children infected through MTCT may not be diagnosed or treated until they show symptoms or reach a certain age. This delay in diagnosis and treatment can result in more advanced HIV disease by the time treatment is initiated, making it more challenging to achieve virological suppression.

Viral load refers to the amount of HIV genetic material (RNA) in a person's blood. It is typically measured in copies of viral RNA per milliliter (copies/mL) of blood. Monitoring viral load is essential in HIV management because it provides valuable insights into the level of viral replication and the effectiveness of ART in controlling the virus. In this study, 73% of the study participants had virological suppression (<1000 copies/mL), indicating that the COGRI ART program needed optimized interventions to achieve the third 90–90–90 target of the UNAIDS. Notably, the virological suppression in ART-treated adults in the general population was at 90.6% as reported in a separate nation-wise survey, suggesting that adults who acquired HIV via MTCT in this study were different in that they maintained high viral loads despite ART. It will be important to assess if they are comparable to age-matched ART-treated adults who acquired HIV in adulthood. A considerable proportion of patients (27%) with high viral load need close follow-up and repeated viral load testing after 3–6 months of enhanced adherence support. Adults, who acquired HIV through mother-to-child transmission (MTCT), may be at increased risk of virological failure due to exposure to the virus from a very early age. This prolonged exposure may lead to a higher risk of early immune system damage and viral seeding throughout the body.These groups would also need evaluation for drug resistance if the high viral loads persist. Therefore, the finding of this study highlighted the importance of improved access to viral load monitoring and prompt action to optimize treatment regimens for patients with high viral loads.

5.1.2 Immunological profiles in ART-treated adults who acquired HIV through MTCT

The CD4 count and other immune markers, such as measurements of other white blood cells like neutrophils, monocytes and total lymphocytes, are frequently combined to provide a thorough evaluation of a person's immune system, especially for PLWH. Overall, CD4 testing

is essential for directing HIV treatment choices, evaluating immune function, and raising the standard of living for HIV-positive people. Low CD4 counts are linked to a higher risk of opportunistic infections, certain malignancies, and other HIV-related consequences. In children and infants, the immune system is still developing and may not respond as effectively to HIV compared to adults with fully developed immune systems. This may result in difficulty in controlling the virus from early age and this may continue into adolescence and adulthood.In this study, immunological failure was defined as CD4 T cell count at or below 250 cells/mm^3. There were 59 individuals (13%) who had immunological failure, suggesting that a significant proportion of adults who acquire HIV through MTCT still have compromised immune systems despite ART. Low CD4 T cell counts might be related to drug resistance and non-adherence to the prescribed ART regimen, leading to incomplete viral suppression and suboptimal immune recovery. Indeed, individuals who had poor viral load suppressions also had lower CD4 T cells counts and lower percentages of lymphocytes.

Notably, in a subset of 17 individuals, immunological failure was observed in the absence of virological failure. Studies have indicated that this could be due to immune activation, which is associated with increased AIDS- and non-AIDS-related morbidity and mortality among individuals with antiretroviral therapy (ART)-mediated viral suppression (Deeks, 2011). Alternatively, individuals may have a slower or less robust immune recovery even with viral suppression if they were diagnosed and initiated ART at a later stage of HIV infection when significant immune damage had already occurred. These discordant observations emphasize the need for comprehensive immunological and clinical evaluation, as well as personalized treatment approaches.

Neutrophils are essential to the body's fight against bacterial infections. Their numbers can vary in HIV-positive individuals with normal numbers early on in the HIV infection and decreased numbers as the illness worsens and CD4 T-cell counts decrease, leaving patients more vulnerable to bacterial infections (Bowers et al., 2014). In this study, 15% of participants had neutropenia, suggesting that adults who acquired HIV through MTCT could have compromised immunity to bacterial infections.

Monocytes are also crucial for immunological protection. They can develop into macrophages, which assist the body in eliminating infections and cellular detritus. Since the infection generally affects the immune system in people with HIV, monocyte numbers may be impacted. Through continuing cell-to-cell transmission of virions, HIV-infected monocytes and

macrophages support viral persistence during infection by serving as a key HIV reservoir and sustaining HIV replication (Knudsen et al., 2022). On the other hand, expansion of monocytes in PLWH has been associated with immune activation. In this study, there were no notable changes in monocytes proportions in the whole cohort. However, we observed higher percentages of monocytes in individuals who had virological failure when compared to those without virological failure, suggesting that poor viral suppression could be driving immune activation in a subset of adults who acquired HIV through MTCT.

5.1.3 Liver Transaminases; AST and ALT

To quickly detect and treat any liver-related issues, regular monitoring of liver function, including liver transaminases, is a crucial component of HIV care. This is particularly important because HIV-infected individuals are exposed to life-long ART treatment. If significant elevations are seen, regular monitoring would be needed. In this study, there were no notable elevations in liver enzymes in ART-treated adults who acquired HIV via MTCT, suggesting that any elevations that could occur are mild and pose little clinical risk.

5.1.4 Opportunistic Infections

Opportunistic infections (OIs) are illnesses that take advantage of a compromised immune system. These infections are frequently present in people with disorders like advanced HIV infection, when the immune system's capacity to fend against infections is impaired. OIs pose a serious threat to HIV-positive individuals, especially those with low CD4 T-cell levels. These infections can affect different regions of the body and range in severity from moderate to severe. The best way to avoid or prevent them is through infection prophylaxis, early diagnosis and adequate treatment. Even with appropriate interventions, Pediatric populations may face adherence challenges, as they rely on caregivers to administer their medication. Ensuring consistent adherence to ART can be more challenging in this age group. Early use of antiretroviral therapy (ART) can also cause the emergence of drug resistance, which in turn can result in opportunistic infections.

As children with HIV grow into adolescence and adulthood, there may be challenges related to transitioning from pediatric to adult HIV care. Stigma and psychosocial factors can play a significant role in pediatric populations. They may face discrimination, bullying, or social isolation, which can affect their mental well-being and adherence to treatment. This could have an impact on their virological and immunological profiles even in their adulthood.These

transition challenges could result in disruptions in care and treatment continuity, potentially leading to virological failure.

HIV-related opportunistic infections include Cryptococcal Meningitis, Tuberculosis, Cytomegalovirus, Toxoplasmosis, Candidiasis among others. Co-infections or comorbidities can contribute to impaired immune recovery despite viral load suppression. This study only considered tuberculosis and Cryptococcus meningitis as opportunistic infection while co-infections such as Hepatitis C and B could also contribute to an impaired immune recovery. Immune senescence, or the aging process of the immune system, can be accelerated by co-infections and comorbidities. Reduced immunological responses and worse immune recovery can be caused by this premature immune system's aging (Lee et al., 2022). Notably, most of the participants with CD4 =< 100 cells/ml were not tested for CrAg as per the Kenya ART guidelines. It will be important for systems to be put in place to implement this guideline.

To achieve the goal of ART treatment in adults who acquired HIV through MTCT, it is important to understand how the disease progresses, their immune responses, effectiveness of the ART regimens as well as the prevalence and patterns of opportunistic infections. Subsequently, identification of the psychosocial support needs of this population, considering challenges of growing up with HIV and stigma, are some key factors that affect treatment adherence, viral suppression rates, and the development of drug resistance. Therefore developing personalized treatment plans, community engagement and education, utilizing digital health tools (such as mobile apps or telemedicine), regular training and updates and multidisciplinary approach involving various specialties will help different healthcare professionals to collaborate seamlessly to provide comprehensive care.

5.1.5 Future Implications

It is essential to recognize the challenges that arise from exposure to the virus from a very early age and tailor healthcare strategies to address the specific needs of individuals who acquired HIV through MTCT. This may include early diagnosis, prompt initiation of ART, close monitoring of adherence, and ongoing support to ensure virological suppression and optimal health outcomes as they transition to adulthood.

Addressing these challenges and tailoring care to the specific needs of individuals who acquired HIV through MTCT, it is possible to reduce the risk of resistance and optimize long-term virological and immunological outcomes while decreasing the risk of opportunistic infections

5.2 Conclusions

Though the majority of HIV-infected adults who have been on ART since childhood had shown viral suppression, the rate of suppression was sub-optimal according to the UNAIDS 90-90-90 target to help end the AIDS pandemic by 2020 while the rate of immunological recovery in the study cohort was significantly high. Hence, early initiation of ART should be strengthened to achieve good virological suppression and immunological recovery. This research is useful in description of potential regions for focused interventions to enhance the health outcomes for individuals who acquire HIV through MTCT. Information on the immunological and virological events that occur in adults who acquired HIV through MTCT is limited, owing to the difficulty in identifying such individuals.

While data may be scarce now, ongoing initiatives to enhance diagnostic techniques and carry out focused research will probably result in a better understanding of the particular health needs and difficulties this particular subgroup of HIV-positive people faces. Clinical management strategies for this population can be improved with the help of new developments in medical technology and greater awareness of MTCT.

Conducting longitudinal studies that track the adherence patterns and drug resistance profiles of individuals who acquired HIV through MTCT from childhood into adulthood can provide insights into how these patterns change over time while assessing adherence behaviors.

Investigatation of psychosocial factors, including stigma, mental health, and social support, that may influence adherence behaviors and drug resistance development.

Further studies on the relationship between early HIV exposure, viral suppression, adherence, drug resistance, and immune recovery and how these factors interact can inform strategies to improve virological and immunological outcomes, thereby promoting optimal health and well-being in this population.

5.3 Recommendations

1. Personalized Treatment Plans that would advocate for personalized ART regimens based on individual patient characteristics, viral load, co-infections, the impact of the virus on key organs, and potential complications of adherence as they age and other factors that might affect treatment outcomes.

2. For optimal results individuals to take an active role in communicating with their healthcare providers, educate themselves about their medications, and take accountability for their treatment plan.

3. Community Engagement and Education: This is an important factor in creating awareness within communities about adherence, HIV monitoring, and addressing stigma associated with HIV as important aspects of HIV programs. Community engagement also supports in identifying the psychosocial support needs of this population.
4. Utilizing digital health tools, such as mobile apps or telemedicine, to provide real-time monitoring of adherence to treatment regimens and allow for the early detection of immunological or virological failure in this technological era.
5. Regular training and updates for healthcare providers on the latest guidelines, protocols, and advances in HIV care to ensure adherence to best practices.
6. Multidisciplinary approach, involving various specialties to help different healthcare professionals to collaborate seamlessly to provide comprehensive care to address issues in this unique group of HIV adults.
7. Focus on children and adolescent since these grow to add into a pool of adults who contracted HIV through MTCT. Focusing on prevention, education, and support for children and adolescents could be relevant. It involves schools, hospitals, NGOs, and community groups in developing a comprehensive support system for them. Through HIV programs, the needs of children, adolescents and young adults affected by HIV can be addressed in a multifaceted manner that incorporates healthcare, education, community involvement, and advocacy for public policy.

REFERENCES

Arts, E. J., & Hazuda, D. J. (2012). HIV-1 antiretroviral drug therapy. *Cold Spring Harbor Perspectives in Medicine*, *2*(4). https://doi.org/10.1101/cshperspect.a007161

Bowers, N. L., Helton, E. S., Huijbregts, R. P. H., Goepfert, P. A., Heath, S. L., & Hel, Z. (2014). Immune Suppression by Neutrophils in HIV-1 Infection: Role of PD-L1/PD-1 Pathway. *PLoS Pathogens*, *10*(3). https://doi.org/10.1371/journal.ppat.1003993

De Santis, G. C., Brunetta, D. M., Vilar, F. C., Brandão, R. A., de Albernaz Muniz, R. Z., de Lima, G. M. N., Amorelli-Chacel, M. E., Covas, D. T., & Machado, A. A. (2011). Hematological abnormalities in HIV-infected patients. *International Journal of Infectious Diseases*, *15*(12). https://doi.org/10.1016/j.ijid.2011.08.001

Deeks, S. G. (2011). HIV infection, inflammation, immunosenescence, and aging. *Annual Review of Medicine*, *62*(5), 141–155. https://doi.org/10.1146/annurev-med-042909-093756

Deeks, S. G., Overbaugh, J., Phillips, A., & Buchbinder, S. (2015). HIV infection. *Nature Reviews Disease Primers*, *1*. https://doi.org/10.1038/nrdp.2015.35

Dong, K. L., Moodley, A., Kwon, D. S., Ghebremichael, M. S., Dong, M., Ismail, N., Ndhlovu, Z. M., Mabuka, J. M., Muema, D. M., Pretorius, K., Lin, N., Walker, B. D., & Ndung'u, T. (2018a). Detection and treatment of Fiebig stage I HIV-1 infection in young at-risk women in South Africa: a prospective cohort study. *The Lancet HIV*, *5*(1), e35–e44. https://doi.org/10.1016/S2352-3018(17)30146-7

Dong, K. L., Moodley, A., Kwon, D. S., Ghebremichael, M. S., Dong, M., Ismail, N., Ndhlovu, Z. M., Mabuka, J. M., Muema, D. M., Pretorius, K., Lin, N., Walker, B. D., & Ndung'u, T. (2018b). Detection and treatment of Fiebig stage I HIV-1 infection in young at-risk women in South Africa: a prospective cohort study. *The Lancet HIV*, *5*(1), e35–e44. https://doi.org/10.1016/S2352-3018(17)30146-7

Getawa, S., Fentahun, A., Adane, T., & Melku, M. (2021). Antiretroviral treatment failure and associated factors among hiv-infected children on antiretroviral therapy: A retrospective study. *HIV/AIDS - Research and Palliative Care*, *13*. https://doi.org/10.2147/HIV.S294046

Gouvêa, A. D. N., Trajano, A. J. B., Monteiro, D. L. M., Rodrigues, N. C. P., da Costa, J. T., Cavalcante, M. B., Auar, D. F., de Gouvea, E. F., & Taquette, S. R. (2020). Vertical

transmission of HIV from 2007 to 2018 in a reference university hospital in Rio de Janeiro. *Revista Do Instituto de Medicina Tropical de Sao Paulo*, *62*, 1–10. https://doi.org/10.1590/S1678-9946202062066

Govender, R. D., Hashim, M. J., Khan, M. A., Mustafa, H., & Khan, G. (2021). Global Epidemiology of HIV/AIDS: A Resurgence in North America and Europe. *Journal of Epidemiology and Global Health*, *11*(3), 296–301. https://doi.org/10.2991/jegh.k.210621.001

HIV. (n.d.). Retrieved September 27, 2023, from https://www.who.int/data/gho/data/themes/hiv-aids

Kassa, G. M. (2018). Mother-to-child transmission of HIV infection and its associated factors in Ethiopia: A systematic review and meta-analysis. *BMC Infectious Diseases*, *18*(1). https://doi.org/10.1186/s12879-018-3126-5

KENPHIA 2018 PREL REP fin_alt2_USAID.indd 1. (n.d.). http://www.nascop.or.ke/KENPHIA

Kenya HIV Prevention and Treatment Guidelines, 2022 Edition. (n.d.).

Knudsen, A. D., Bouazzi, R., Afzal, S., Gelpi, M., Benfield, T., Høgh, J., Thomsen, M. T., Trøseid, M., Nordestgaard, B. G., & Nielsen, S. D. (2022). Monocyte count and soluble markers of monocyte activation in people living with HIV and uninfected controls. *BMC Infectious Diseases*, *22*(1). https://doi.org/10.1186/s12879-022-07450-y

Larmarange, J., Diallo, M. H., McGrath, N., Iwuji, C., Plazy, M., Thiébaut, R., Tanser, F., Bärnighausen, T., Pillay, D., Dabis, F., & Orne-Gliemann, J. (2018). The impact of population dynamics on the population HIV care cascade: results from the ANRS 12249 Treatment as Prevention trial in rural KwaZulu-Natal (South Africa). *Journal of the International AIDS Society*, *21*(S4), 6–15. https://doi.org/10.1002/jia2.25128

Lee, K. A., Flores, R. R., Jang, I. H., Saathoff, A., & Robbins, P. D. (2022). Immune Senescence, Immunosenescence and Aging. In *Frontiers in Aging* (Vol. 3). Frontiers Media S.A. https://doi.org/10.3389/fragi.2022.900028

Li, W., Koay, A., Kose-Otieno, J., & Rakhmanina, N. (n.d.). *HIV Drug Resistance in Children and Adolescents: Always a Challenge?* https://doi.org/10.1007/s40471-021-00268-3/Published

McKinney, R. (2006). Antiretroviral therapy. *Handbook of Pediatric HIV Care, Second Edition*, *28*(3), 335–359. https://doi.org/10.1017/CBO9780511544781.013

McMichael, A. J., Borrow, P., Tomaras, G. D., Goonetilleke, N., & Haynes, B. F. (2010). The immune response during acute HIV-1 infection: Clues for vaccine development. *Nature*

Reviews Immunology, *10*(1), 11–23. https://doi.org/10.1038/nri2674

O Murchu, E., Marshall, L., Teljeur, C., Harrington, P., Hayes, C., Moran, P., & Ryan, M. (2022). Oral pre-exposure prophylaxis (PrEP) to prevent HIV: a systematic review and meta-analysis of clinical effectiveness, safety, adherence and risk compensation in all populations. *BMJ Open*, *12*(5), e048478. https://doi.org/10.1136/bmjopen-2020-048478

Omari, M., & Ouifki, R. (2010). *Oscillations in a Model for HIV Infection with Three Intracellular Delays and RTI: Delays Can Induce Viral Blips*.

Qin, F., Jiang, J., Qin, C., Huang, Y., Liang, B., Xu, Y., Huang, J., Xu, Z., Ning, C., Liao, Y., Zang, N., Lai, J., Wei, W., Yu, J., Ye, L., Qin, X., & Liang, H. (2019). Liver damage in patients living with HIV on antiretroviral treatment with normal baseline liver function and without HBV/HCV infection: An 11-year retrospective cohort study in Guangxi, China. *BMJ Open*, *9*(4), 1–10. https://doi.org/10.1136/bmjopen-2018-023140

Sharp, P. M., & Hahn, B. H. (2011). Origins of HIV and the AIDS pandemic. *Cold Spring Harbor Perspectives in Medicine*, *1*(1), 1–22. https://doi.org/10.1101/cshperspect.a006841

Shaw, G. M., & Hunter, E. (2012). HIV transmission. *Cold Spring Harbor Perspectives in Medicine*, *2*(11). https://doi.org/10.1101/cshperspect.a006965

Terms, A. (2021). *of HIV/AIDS-Related Terms 2021 • 9*. 180.

UNAIDS and AIDSinfo. (2021). Country factsheets Kenya. *Unaids*, 1–6. https://aidsinfo.unaids.org/%0D

Vijayan, K. V., Karthigeyan, K. P., Tripathi, S. P., & Hanna, L. E. (2017). Pathophysiology of CD4+ T-Cell depletion in HIV-1 and HIV-2 infections. In *Frontiers in Immunology* (Vol. 8, Issue MAY). Frontiers Media S.A. https://doi.org/10.3389/fimmu.2017.00580

WHO releases HIV drug resistance report 2021. (n.d.). Retrieved September 27, 2023, from https://www.who.int/news/item/24-11-2021-who-releases-hiv-drug-resistance-report-2021

Yu, W., Hu, X., & Cao, B. (2021). *Viral Infections During Pregnancy: The Big Challenge Threatening Maternal and Fetal Health*. https://doi.org/10.1097/FM9.0000000000000133

Zhang, F., Sun, M., Sun, J., Guan, L., Wang, J., & Lu, H. (2015). The risk factors for suboptimal CD4 recovery in HIV infected population: An observational and retrospective study in Shanghai, China. *BioScience Trends*, *9*(5), 335–341. https://doi.org/10.5582/bst.2015.01107

APPENDICES

APPENDIX I: Data Collection Tool

1) **CCC No. of the patient:** .....

2) Status of the patient

Active ( ) Lost to Follow Up ( ) Relocated ( ) Exit> 18 years ( ) Transfer out ( ) Deceased ( )

3) **COGRI Site** (*Tick appropriately*)

Nyumbani Kibera Kangemi Kawangware Dandora Dagoretti Kariobangi Zimmermann Kitui Village Mukuru

4) **Patient Information** (*information to be retrieved from the Lab information system for year 2018*)

Variables			
a) Age (Date of Birth)			
b) AST			
c) ALT			
d) HIV Viral load (HIV RNA copies/ml)			
e) CD4 Counts (µL)			
f) Lymphocyte Absolute counts			
g) Neutrophils Absolute counts			
h) Monocytes Absolute counts			
i) Opportunistic Infections (Specify)			

Tool filled by:

Name:..... ..... Date:.....

Signature.....

APPENDIX II: Risks and Benefits

Risk

There was no risk to the participants since the study used archived data from the Laboratory information system and other medical records.

Benefits

To ensure that the outputs from this research inform practice and hence maximize the benefit to the COGRI health team, patients, and other stakeholders, the dissemination strategy will involve the use of evidence to translate knowledge into practice. This will be done through a presentation in COGRI medical meeting that will have participants from the four COGRI programs, as well as presentations to COGRI clinicians and the Laboratory team. The study findings summary will also be shared with the COGRI. The impact would be evidence-based decisions to ensure better HIV monitoring and this would, in turn, benefit the clients through a reduction in immunological failure.

The study findings will also be published in a peer-reviewed scientific journal to inform policy globally.

Confidentiality of research data

To protect the participant's rights and welfare, their data was stored in a safe password-protected computer. Direct identifiers were only used to identify the data required, then this was coded. The data collected was only used for this study.

Ethical consideration: Ethical issues could only arise from data handling; however, this was protected by adhering to biosecurity principles. The project was approved by the KNH-UoN Ethics committee. A letter of approval from Children of God Relief Institute was issued to allow the collection of data.

Contact Person

In case of any inquiries regarding the research contact;

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APPENDIX III: Approval Letter from Children of God Relief Institute

Sr. Mary Owens, IBVM.
The Executive Director,
Children of God Relief Institute – Nyumbani.
P.O. Box 24970-00502,
Nairobi.
05th May 2022

RE: REQUEST FOR ACCESS TO THE COGRI CLINICAL INFORMATION.

With reference to the above subject, as a Master's student in Tropical and infectious diseases at the University of Nairobi, I am required to write a thesis as a requirement for graduation.
It is in this regard that I request you to allow me to access the COGRI clinical information that could be through the laboratory information system, patient's request forms, other medical records, or files.

The outcome of my research will be availed to your office and this could be used to inform the COGRI programs.

Yours sincerely,
Sr. Susan W Kang'ethe
Lab Quality Manager,
Nyumbani Lab

Approved: Mary Owens IBVM
5th May, 2022

SR. MARY OWENS, IBVM
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APPENDIX IV: Approval letter from KNH-UoN Ethics Committee

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Ref: KNH-ERC/A/225

5th June, 2023

Susan Wanjiru Kang'ethe
Reg No. W64/33359/2019
Dept. of Medical Microbiology
Faculty of Health Sciences
University of Nairobi

Dear Susan

ETHICAL APPROVAL-RESEARCH PROPOSAL: A RETROSPECTIVE DESCRIPTIVE STUDY OF IMMUNOLOGICAL AND VIROLOGICAL PROFILES OF ADULTS WHO ACQUIRED HIV IN CHILDHOOD THROUGH MOTHER-TO-CHILD TRANSMISSION (P76/01/2023)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P76/01/2023.** The approval period is 5th June 2023 –4th June 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Protect to discover

APPENDIX V: Approval National Commission for Science, Technology & Innovation

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: 234127

Date of Issue: 24/August/2023

RESEARCH LICENSE

This is to Certify that Sr.. Susan Wanjiru Kang'ethe of University of Nairobi, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Nairobi on the topic: A retrospective descriptive study of Immunological and Virological profiles of adults who acquired HIV in childhood through mother-to-child transmission for the period ending : 24/August/2024.

License No: NACOSTI/P/23/28697

234127

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

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See overleaf for conditions