KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY:

SCHOOL OF MEDICAL SCIENCE

DEPARTMENT OF CLINICAL MICROBIOLOGY

DETERMINATION OF HAEMATOLOGICAL AND BIOCHEMICAL ABNORMALITIES IN HIV/AIDS INFECTED PATIENTS RECEIVING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY AT THE EFFIANKWANTA REGIONAL HOSPITAL IN THE WESTERN REGION.

BY

SAMUEL KWADWO AFARI

A THESIS SUBMITTED TO THE DEPARTMENT OF CLINICAL MICROBIOLOGY, COLLEGE OF HEALTH SCIENCES, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF DEGREE OF

MASTER OF SCIENCE

IN

CLINICAL MICROBIOLOGY

SEPTEMBER, 2016

DECLARATION

I hereby declare that this submission is my own work towards the M Sc. and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the university, except where due acknowledgement has been made in the text.

SAMUEL KWADWO AFARI (PG9954713) ……. ……..……

Student Name & ID No Signature Date

Certified by:

DR. T. B. KWOFIE ……..…. ……..…..……

Supervisor's Name Signature Date

Certified by:

DR. T. B. KWOFIE ……. ……..……

Head of Dept. Name Signature Date

DEDICATION

This work is devoted to the glory of the Almighty God, to every individuals living with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome and to all participants in the fight against this plaque.

ACKNOWLEDGEMENTS

I wish to acknowledge Dr. Theophilus B. Kwofie Head of Department of Clinical Microbiology, KNUST medical School and also my Supervisor for his supervisory role. My Appreciation goes to Dr. Paul Kwaw Ntodi Medical Director of EffiaNkwanta Regional Hospital for allowing me to do the research at the hospital, Dr. Roland Sowah, Western Regional Coordinator of AIDS and head of Comprehensive Care Centre (CCC),

for allowing me to use the facility for my study and the PCR laboratory at the facility to run the viral load samples. I cannot also forget the Nurses at the CCC facility for their support especially sister Georgina. I am highly indebted to Mr. Kofi Mensah Regional chairman of the Biomedical Laboratory Scientist Association and head of Public Health Reference Laboratory for using the lab for my studies and for his words of encouragement and regular support. Sister Irene Amedzro and Mr. Amoako for their immense contributions on how to use the PCR devices. Mr. Samuel Asamoah Regional Biomedical Scientist and Head of laboratories for allowing me to run my Full Blood Count Parameters and Biochemical markers at the main lab. I further wish to acknowledge Mr. Nana Ntim the administrator of Axim Government Hospital for his immense contribution of helping me get study leave for the programme. My dear mother Georgina Opare and my lovely daughter Evelyn Odamea Afari for their prayers for me and not forgetting my colleagues at my former work place Axim Government Hospital laboratory for their diverse contributions and Madame Merridya Musa Hawa for her encouragement. The last but not the least is my former Municipal Health Director Dr.
Tachie Mensa for advising to go for further studies.

ABSTRACT

The introduction of HAART has led to a significant improvement in prolonging survival of HIV-infected patients on treatment in resource-limited areas. Nevertheless, the key problem of HAART that long-term use has the potential to cause haematological and biochemical abnormalities that may be life-threatening. These significant difficulties sometimes permit change or discontinuation of ART. Data on the prevalence of the above complications in Ghana is limited. The current study assessed the haematological and biochemical abnormalities in HIV/AIDS infected persons that may be associated with the administration of HAART and their virological responses of which 200 seropositive HIV patients were tested pre and post HAART based on clinical laboratory biomarkers in a comparative cross-sectional study. Results were matched for gender, age and HAART status. The data was analyse using SPSS, Paired sample t-test and One-way ANOVA.The prevalence of haematological cytopenias (Anaemia, leucopenia, neutropenia, lymphopenia and thrombopenia) which were classified into mild, moderate and severe saw significant reduction after treatment. The degree of cytopenias among gender was higher in females as compared to male post treatment. There was significant change in the levels of ALT and ALP which may indicate an association with hepatocellular injury with HAART treatment in participants with HIV infection. When creatinine clearance/glomerular filtration rate (GFR) was measured to determine degree of renal dysfunction and the prevalence of chronic kidney disease among HIV seropositive before and after medication. There was a reduction in renal dysfunction and chronic kidney disease when CKD-EPI equation was used post-HAART (18%16.5%).This shows that renal pathology appeared to have improved after HAART, being an indication of ART ability to resolved renal disorders. The average viral load significantly reduced from 137966.30±4.05 in mean (copies/ml) to 2037.49±22.86 (copies/ml) after treatment (p-<0.0001). Viral load decrease significantly after HAART among males and females, [176441.20±3.65 vs 2641.19±24.17 and 128558.26±4.16 vs 1891.47±22.73] (copies/ml) respectively (p-<0.0001, p-0.0001). HAART had a **weak effect** on viraemia (n^2-0.028), **moderate effect** on haemoglobin (η2 - 0.048), **weak effect** on total protein (n^2-0.041) and **moderate effect** on serum albumin (η2 - 0.07). HAART therefore had a positive impact on viraemia, haematological and biochemical parameters as compare to HIV infection. Immunological status must be determined through CD4 count test.

LIST OF ACRONYMS

ABC:	Abacavir
AIDS:	Acquired Immunodeficiency Syndrome
ART:	Antiretroviral therapy
AZT/ZDV:	Zidovudine
CD4:	Cluster of Differentiation 4
CDC:	Centre for disease control
DNA:	Deoxyribonucleic acid
D4T:	Stavudine
EFV:	Efavirenz
FTC:	Emtricitabine
HAART:	Highly Active Antiretroviral Therapy
HIV:	Human Immunodeficiency Virus
LPV/r:	Lopinavir/ritonavir
NACP:	National AIDS Control Program
NRTI:	Nucleoside reverse transcriptase inhibitor
NNRTI:	Non-nucleoside reverse transcriptase inhibitor
NVP:	Nevirapine
PI:	Protease inhibitor
PMTCT:	Prevention of mother-to-child transmission
3TC:	Lamivudine
TDR:	Transmitted Drug Resistance **tRNA:** transfer ribonucleic acid.
VCT:	Voluntary counseling and testing
WHO:	World Health Organization

TABLE OF CONTENT

LIST OF FIGURES

CHAPTER ONE

INTRODUCTION

1.0. BACKGROUND OF THE STUDY

Human Immunodeficiency Virus (HIV) is the cause of AIDS. There is a gradual impairment to one's immune system as a characteristics of the infection, resulting in a number of immunological, haematological, biochemical problems and opportunistic infections *(Stevenson, 2003).* Cellular CD4 T-lymphocyte destruction is the hallmark of HIV infection which occurs through several processes such as dysregulation of cytokines, cytotoxic T-lymphocyte responses, HIV induced autoimmune reactions HIV induced cytolysis, and others *(Crum-Cianflone et al., 2009).* The second most common causes of mortality in HIV/AIDS individuals has been found to be haematological problems and are largely noticeable with cytopoenia *(Moyle, 2002).* The frequently seen haematological disorder is anaemia and is also a major predictor of HIV advancement to AIDS, and subsequently death. *(Odunukwe et al., 2005).*

In ART-treated and untreated HIV/AIDS patients, diverse types of immunological, biochemical and haematological disorders are common. These may happen as a consequence of drug used for HIV infection and its related conditions, HIV infection itself and sequelae of HIV-associated opportunistic infections. Whereas, anaemia, leukocytopaenia, neutropenia, Thrombocytopenia, depletion of the CD4 cells and changes in biochemical indicators such as Bilirubin, Electrolytes, Creatinine, Blood Urea, ALT, ALP, AST, and Albumin are the commonest haematological and biochemical disorders resulting from HIV infection. ART use can positively or negatively have impact on these disorders *(Ibeh et al 2013).*

According to *Pereira and Paridaen (2004),* the advent of drug expansion programmes by pharmaceutical companies, research institutions and state agencies, has led to the production of numerous effective anti-HIV drugs called Antiretroviral drugs. Presently, a combination of this therapy known as HAART which is highly active antiretroviral therapy is recognised as gold standard treatment for the treatment of HIV infection. The initiation of highly active antiretroviral therapy, normally made up of a blend of two or more antiretroviral drugs has come to advance the quality of life of persons living with HIV/AIDS. HAART have led to a decline in the progression of HIV infection to AIDS *(Palella et al., 1998).*

But, researches have shown that administration of the HIV drugs comes with adverse toxic ramifications, which include but are not limited to, diarrhoea, nausea, anaemia, neutropenia, increase in bilirubin, elevation of Amylase enzyme and cytopoenia *(Pluda, Mitsuya, & Yarchoan, 1991).*

The present study therefore, evaluated the possible haematological and biochemical abnormalities that may be related with HAART.

1.1. PROBLEM STATEMENT

Antiretroviral drug has considerably improved prognosis of HIV and AIDS infections by repairing immune system destruction and regulating opportunistic infections. Nevertheless, HIV treatment outcomes in toxicities that complicate management and increases the cost of health care. Antagonistic effects have been stated with all ART and are part of the common motives for changing or suspending drugs and also for therapy non-adherence *(O Brien, 2003).* The highly active antiretroviral drug side effects are now an essential public health difficulty which has contributed to more than 50% of haematological and biochemical abnormalities. Data on HAART abnormalities are abundant, but they are inconsistent and hence more vigorous studies are required *(Kramer et al.., 2007).* The dependence of HIV patients on HAART for longer periods of time, leads to an increase in HAART-related metabolic syndromes leading to haematological disorders such as anaemia and biochemical toxicities such as hepatoxicity renal injury. Couple of Studies has been conducted in Komfo Anokye Teaching hospital but no such study has been carried out at EffiaNkwanta Regional hospital, hence, a research study is being done to clarify some possible abnormalities that may be associated with HAART on the haematological and biochemical parameters.

1.2. JUSTIFICATION OF THE RESEARCH

Majority of HIV/AIDS incidence are recorded in Sub-Saharan Africa. In Ghana, Human Immunodeficiency Virus remains to be a generalized epidemic. This disease continues to devastate the population, the productive capacity and economic growth in Ghana. The first case of HIV/ AIDS was reported in Ghana in 1986, *(Cote A.M, Dzokoto, Asamoah-Adu et al, 2004).* According to Ghana AIDS Commission, the estimated number of adults and children living with HIV as of 2014 is 150,000 and at incidence

rate of 0.8%. The prevalence rate of HIV type I remains dominant at 97.1%, HIV type I and II is at 2.1% and HIV type II remains 0.8% as at 2013. HIV/AIDS elimination in Ghana, however, has rapidly progressed since the introduction of HAART in 2003 which now serves as the benchmark for treatment and management of HIV/AIDS. This highly active antiretroviral therapy has changed HIV infection from a devastating fatal disease to a chronic manageable disease and also very active in suppressing systemic HIV viral load.

Records from the Comprehensive Care Center at the EffiaNkwanta hospital shows that Naive HIV patients shows a lot of abnormal indices from their haematological and biochemical biomarkers but there is no information with regards to toxicity effect produce as a result of the use of the highly active antiretroviral therapy. It is against this conditions that the study was carried out to assess the haematological and biochemical toxicities among the HIV/AIDS patients on HAART.

1.3. AIM OF RESEARCH

The main aim of the study is to determine the haematological and biochemical abnormalities of HIV/AIDS infected patients that may be associated with the administration of HAART and their virological responses at the EffiaNkwanta Regional Hospital in the Western Region of Ghana.

1.4. SPECIFIC OBJECTIVES

1. To determine the haematological and biochemical responses of HIV/AIDS patients before, during and after initiating the HAART.
2. To determine the virological responses of HIV/ AIDS patients on HAART.

CHAPTER TWO

LITERATURE REVIEW 2.0. HUMAN IMMUNODEFICIENCY VIRUS (HIV)/ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS

HIV belongs to the retrovirus family. HIV/AIDS affects the human immune system of infected persons by destroying T-lymphocytes which the body depends to fight against infections *(Reviewed by Alexander Kramer & Klaus Krickeberg et al, 2000).* The two different serotypes of human immunodeficiency virus are HIV Type 1 and HIV Type

2. The HIV type 1 is the key cause of acquired immunodeficiency syndrome (AIDS) globally while, HIV type 2 is found mostly in West Africa and vertical transmission is uncommon *(See Sanders et al.., 2007)*

AIDS is the late stage of HIV infection, a disorder characterized by destruction of CD4+ T cells which help the body fight diseases *(GASCOP, 2002)*. Early infection with HIV may results in flu-like symptoms, infected individuals characteristically may show no symptoms for many years but as HIV replicate in the body, infected individuals begin to show signs and symptoms such as, shingles, tuberculosis, herpes simplex virus, oral or vaginal thrush and Kaposi's sarcoma *(See Granich, R. M., Gilks et al, 2009).* HIV is transferred predominantly through unprotected sexual contact (comprising Anal and Oral sex), intravenous drug user, haemophiliacs giving factor 8, blood transfusions, subcutaneous needles and from mother to child through perinatal period, delivery, or breastfeeding *(Reviewed by Markowitz et al, 2007).* Specific bodily fluids, such as saliva and tears, cannot spread HIV *(CDC HIV & Transmission, 2003).* HIV infection can primarily be prevented through safe sex and this becomes an important approach to regulate the transmission of the virus. HIV has no cure or vaccine; yet, ART usage can slow the course of the disease and might lead to a near-normal life expectancy. Although, ART treatment decreases the risk of death and difficulties from the disease, these drugs are costly and have adverse effects. The average existence time after infection with HIV is projected to be 9 to 11 years if a patient is not treated, based on the HIV subtype. *(UNAIDS, AIDS epidemic, 2007*).

2.1. Classifications

Based on surveillance purposes HIV is classified into two main clinical staging systems and these are: **The World Health Organization disease staging system for HIV infection and disease** *(WHO/HIV/2005.02)* and **the Center for Disease Control classification system for HIV infection** *(See Schneider et al, 2008).* The Center for Disease Control classification system is more often accepted in advanced countries. The World Health Organization staging system do not need laboratory investigations, it is suitable to be used in emerging countries where there is constraint in resources and is also serves as a support guide in medical management. The two schemes permit evaluation for statistical reasons in spite of their differences *(Reviewed by Mandell & Schneider et al, 2010).*

The World Health Organization classification uses the following categories: **Primary HIV infection**: Can be related to acute retroviral syndrome or can be asymptomatic.

Stage I: There is asymptomatic HIV infection with a CD4+ T cell count greater than 500 cells per microliter of blood. This may comprise generalized lymph node enlargement.

Stage II: There is mild symptoms which comprises minor mucocutaneous appearances and frequent upper respiratory tract infections with a CD4 count of less than 500 cells/µl.

Stage III: There is a progressive symptoms including inexplicable chronic diarrhoea for more than a month, serious bacterial infections comprising tuberculosis of the lung, and a CD4 count of less than 350 cells/µl.

Stage IV or AIDS: There is severe symptoms which comprise candidiasis of the oesophagus, trachea, bronchi or lungs, toxoplasmosis of the brain, and Kaposi's sarcoma. There is also CD4 count of less than 200 cells/µl *(WHO/HIV/2005.02).* CDC also made a classification scheme for HIV, and restructured it in 2008 *(Reviewed by Schneider et al, 2008).* This scheme categorises HIV infections with respect to CD4 count and medical symptoms *(Schneider et al, 2008)* and defines the infection in three stages:

Stage 1: There is a CD4 count ≥ 500 cells/µl and no conditions for AIDS defining.

Stage 2: There is a CD4 count 200 to 500 cells/µl and no conditions for AIDS defining.

Stage 3: There is a CD4 count ≤ 200 cells/µl or conditions defining AIDS.

2.2. Diagnosis of HIV infection

The presence of HIV infection in persons is determined sorely through the use of laboratory test. The various body fluids in which HIV can be found are serum, plasma, vaginal fluids, blood among others. There is an algorithm which has been recognised by WHO-UNAIDS use for several screening tests, surveillance and diagnostic purposes *(WHO Project ICP, 2009).*

Within four to six weeks of infection, antibodies to HIV are detectable using the serological test. Practically, all infected persons with HIV within six months have HIV antibodies persisting for a generation, once it appears in blood *(Reviewed by Bunnel and Cherutich, 2008).* The means in which HIV can be diagnosed is through detection of antibodies to HIV, P24 HIV antigen, HIV nucleic acid (RNA/proviral DNA) in clinical samples *(WHO Project ICP, 2009).*

Serological tests are the most mainly method used in diagnosis of HIV infection. It can be executed easily in most laboratories, economical and rapid. The enzyme- linked immune-sorbent assay (ELISA) is the benchmark investigation test used to detect HIV antibodies of the patients where a blood is mixed with proteins from HIV *(WHO Project ICP, 2009).* There will be an attachment if the blood contains HIV proteins, producing a colour change in the mixture. The test is highly reliable when it is done two to three months after infection with the virus. Sensitivity of HIV test kits such as HIV 1-2.0 Card Test predominantly used in Ghana are very high, but, falsepositive results can be produced. Therefore, HIV test kit called Rapid HIV antibody test (Oral Quick) is used to confirm a positive ELISA HIV. These test can detect lower levels of HIV antibodies within 15-20 minutes. A blood sample is smeared to a paper strip containing HIV proteins in the test, and if HIV antibodies are present, they bind to the HIV proteins, generating a color change on the paper *(See Bunnel and Cherutich, 2008).*

ELISA (which detects antibodies) and the Western Blot test (detects antigen or P24 HIV antigen) combination is more than 99.9 percent precise in identifying HIV infection within 12 weeks after exposure. After HIV infection is confirmed from tests the health status of the infected individual's immune system is checked periodically by measuring CD4 cell counts and viral load in the blood. Viral load test qualitatively and quantitatively detects the virus in the infected persons and is determined using polymerase chain reaction (PCR) test. The rate of HIV growth in an infected person is determined by the viral RNA. *(CDC, 2009).* Increasing viral load corresponds to progressive loss of CD4 cells and a deteriorating state of the disease signifying that the immune system is progressively becoming debilitated or impaired.

2.3. Modes of Transmission

The transmission of HIV virus can be determined by the quantity of infectious virus in a body fluid and the degree of contact by that body fluid. Studies done during 1981 and 1982 first establish that the main routes of transmission of AIDS were through sexual interaction and contaminated blood *(Jaffe et al 1983).* The syndrome was primarily described in homosexual and bisexual men *(Reviewed by Gottlieb, Masur, Siegal et al, 1981)* and intravenous drug users, but its occurrence as a result of heterosexual activity was soon recognized as well *(Harris et al 1983).* Moreover, it became real that transfusion receivers and haemophiliacs might contract the illness from blood or blood

products and also mothers could transfer the causative agent to new born babies. The three main means of transmission have not changed. That is through blood, sexual contact, and mother-to child *(See Brookmeyer, Stone burner, 1991)* and can be clarified to a greater extent by the comparative concentrations of HIV in various body fluids.

A study in Mombasa, Kenya, shows that men who had sex only with other men were 43.0% who tested positive to HIV, as compared with men who testified having sex with both men and women at 12.3% (*Sanders et al.., 2007).*

2.4. Risks Groups

Gay, heterosexuals, injection drug users (IDUs) and bisexual men recorded more than half of new HIV infection cases *(CDC HIV Surveillance Report, 2012).*

2.5. Life Cycle of HIV

For individuals to understand the life cycle of HIV, it is essential for one to be conversant with the structure of the virus. It is an established scientific fact that HIV in common with other retroviruses has the enzyme reverse transcriptase and comprises of a lipid bi-layer membrane surrounding the capsid. It also has a surface glycoprotein molecule (gp.120) with a robust attraction for CD4 receptor protein which can be seen mostly in T helper/inducer lymphocytes. Macrophages and monocytes similarly have the probability of possessing CD4 receptors and can therefore become points of entry for HIV *(Reviewed by Garred P, 1998).*

Scientific facts have proven that the process of HIV entry is more complex than originally supposed to be and that in addition to CD4 attachment, successive binding to co-receptors such as CCR-5, CCR-2 or CXCR-4 and membrane fusion occur. After penetrating the host cell, the virus sheds its outer coat and releases its genetic material via the reverse transcriptase enzyme. The RNA virus is then transformed to DNA via nucleosides through reverse transcriptase enzymes mediation process (Figure 2.1). The proviral DNA virus is incorporated into the host genome in the cell nucleus by the integrase enzymes. It then goes through transcription and translation which enables the production of new viral proteins. The new viral particles are assembled and bud out of the host cells and finally matured into infectious virions under the mediation of protease or proteinase enzyme *(Garred P, 1998).*

Immediately after infection there is a very high rate of viral turnover after which equilibrium is established (Figure. 2.2). At this stage the infection may appear to be clinically latent, but up to 10,000,000 million new virions are produced each day. When chronic infection progresses, all cells having CD4 receptors (mainly the T helper lymphocytes) are depleted from the body in the absence of antiretroviral drug intervention. However, with ARV drug interference viral load is suppressed resulting in immune system rebound (Figure. 2.3). The T helper cell is often considered to be the performer of the immune system *(Garred P, 1998),* and thus as this cell is depleted the individual becomes susceptible to a myriad of infections and tumours. The rate at which this immunosuppression progresses varies between individuals, but the full understanding of it is lacking. However, it is well documented that certain persons quickly develop advance immunosuppression while others possibly will have been living with HIV for many years while sustaining a relatively complete immune system. It is possible that host and environment related factors contribute to this variation.

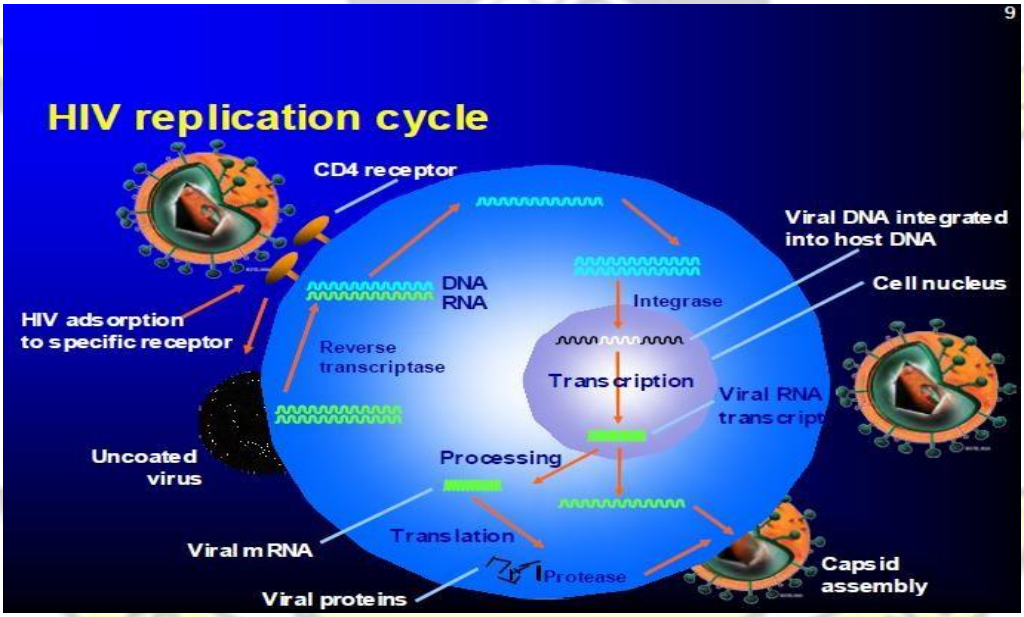


Figure 2.1. The process of attachment of HIV to host CD4 cell and various steps in the replication process. Source: *(Reviewed by Garred P, 1998).*

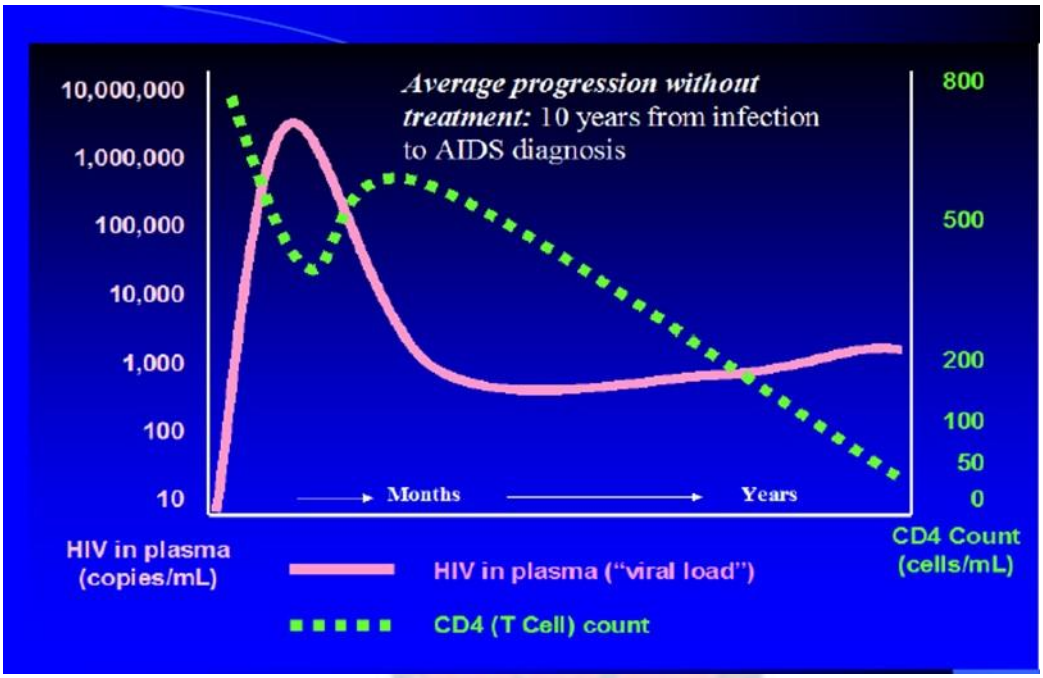


Figure 2.2: The relationship between CD4 count and the viral load without antiretroviral drug intervention. Source: *(Garred P, 1998).*

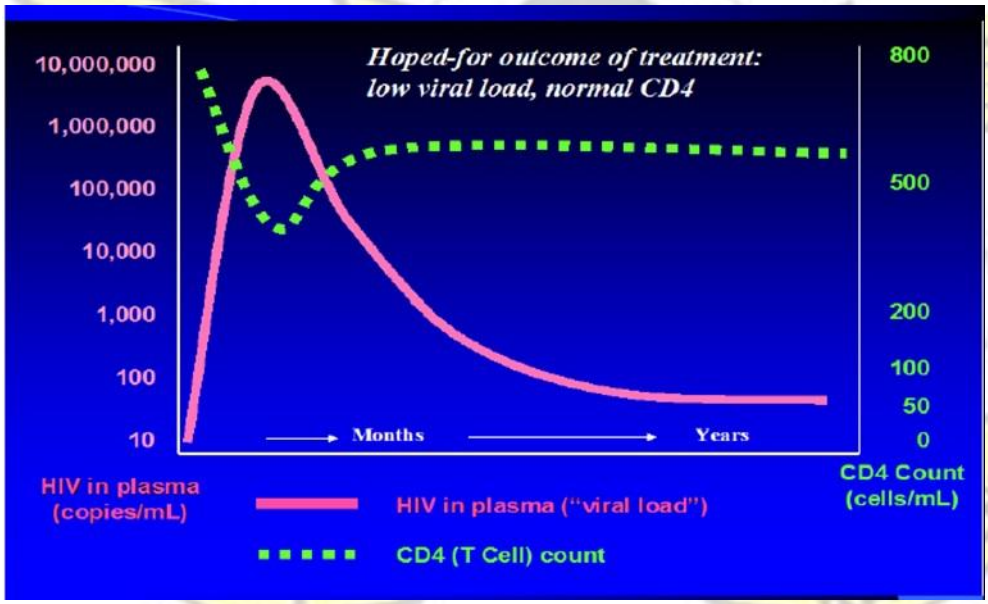


Figure 2.3: The relationship between CD4 Count and viral load with antiretroviral drug intervention. Source: *(Garred P, 1998).*

2.6. Structure of Human Immunodeficiency Virus (HIV)

Particle of HIV is sphere-shaped and is 1/10,000 nm in diameter. HIV is an enveloped retrovirus.

Elementary structure of the HIV is made up of:

- The viral envelope, the exterior coat of the virus, comprises of two layers of lipids; dissimilar proteins are fixed in the envelope of the virus, forming "spikes" containing the outer glycoprotein (gp) 120 and the transmembrane gp41. The lipid membrane is copied from the host cell in the course of the budding process (formation of new particles). Gp120 is required to attach to the host cell, and gp41 is needed for the cell fusion process.
- The HIV matrix proteins (including p17 protein), sandwiched between the core and envelope.
- The viral core, is made up of the viral capsule protein p24 which surrounds two single strands of HIV RNA and the enzymes required for HIV replication, made up of reverse transcriptase, integrase and protease enzymes; there are three viral genes out of the nine viral genes and these are gag, pol and env, which comprises the information required to make structural proteins for new viral particles.

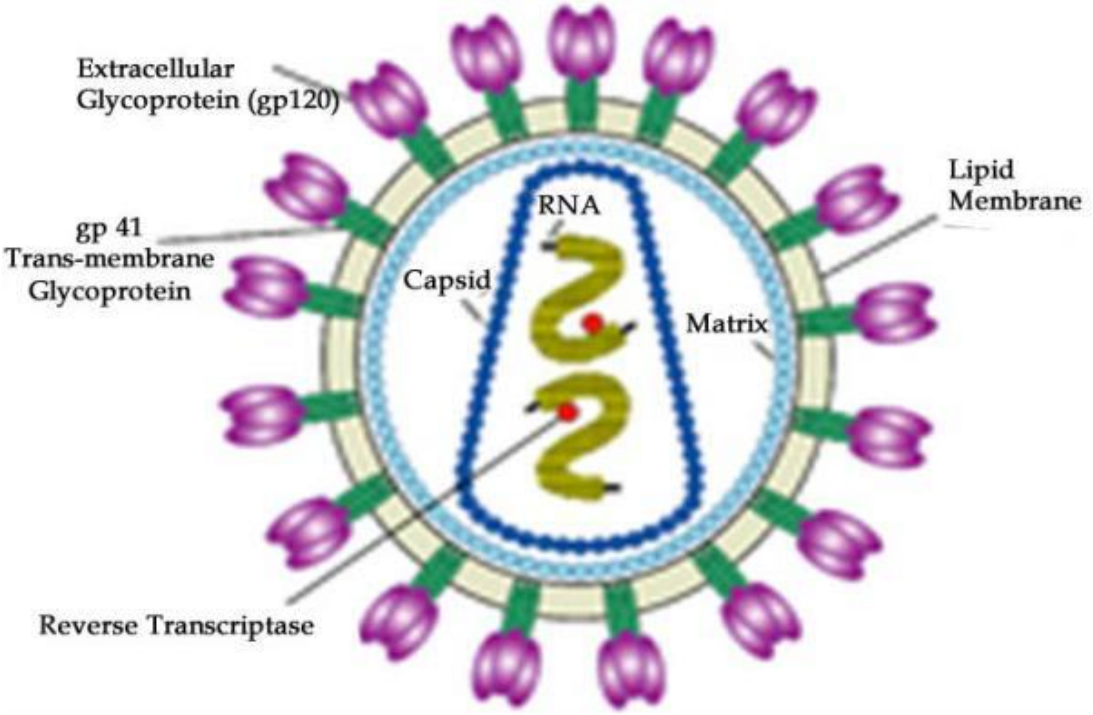


Figure 2.4: The structure of Human Immunodeficiency Virus (HIV). Single stranded RNA are shown within the nucleus with two molecules. Viral RNA is transformed to DNA by the reverse transcriptase enzymes. Source: *(Garred P, 1998).*

2.7. HIV Replication

Replication of HIV start with binding (Attachment) of the glycoprotein of the virus spikes to the Cluster of differentiation-4 surface receptor protein. There is precise communication between the viral gp120 envelope glycoprotein and the CD4 cell-surface receptor.

After binding, a process of membrane fusion, helped by the viral gp41 envelope glycoprotein and by the fusion (CXCR4) and CCR5 proteins, marks the introduction of the HIV core particle into the cytoplasm *(Reviewed by Saville, Constantine et al,2001).* Once it enters the cytoplasm, the reverse transcriptase uses the virion tRNA as a primer and produces a complementary negative stranded DNA. The reverse transcriptase which acts as a ribonuclease H, changes the RNA genome, and produces the positive strand of DNA (complementary DNA) with LTRs at the ends *(Reviewed by Murray RP et al, 2002)*. The double stranded complementary DNA is delivered to the nucleus and then integrated into the host chromosome with help of a viral encoded, virion-carried enzyme, Integrase. Once integrated, the viral DNA is copied as a cellular gene by the host RNA polymerase II. Transcription of the genome gives a complete length RNA, which can be accumulated into new virions *(Reviewed by Saville, Constantine et al, 2001).* The split viral mRNA transcriptase provide growth to env and to the controlling tat, rev, and nef proteins. The Unsplite transcriptase encode the Pr55 gag and Pr160 gag-pol fusion proteins and also help as genomic RNA enveloped into newly assembling virus particles *(Reviewed by Saville, Constantine et al, 2001)*. HIV elements then assembled on the host cell surface and gain viral env proteins as they bud through the host- cell membrane. The viral gag and gag- pol polyproteins are cleaved by competing protease during or just after budding, generating complete infectious virions *(Reviewed by Saville, Constantine et al, 2001).*

2.8. HIV Infection Immune Responses

Individuals with HIV infection produce an effective immune response to the virus in the early few months of infection. But, with time this response will show ineffectiveness.

Two forms of responses are known: Cellular and Humoral responses.

Cellular response is the action of the CD4 and CD8 T cells, similarly identified as cytotoxic lymphocytes.

Humoral response deals with antibody production and it activity.

CD8 T cells work against HIV in two diverse ways in the course of primary infection:

- Killing of HIV-infected cells directly.
- By the production of chemokine's as an anti-HIV molecule.

Whereas in most HIV infected patients, CD8 T cell counts drop again during infection, selected patients continue to show robust HIV-specific CD8 T cell reactions which regulate viral load. CD8 T cells exhibit a critical role in determining the rapidity of HIV disease progression.

Cell ratio of CD4/CD8: To determine a better image of disease progression, it is desirable to measure the cell ratio of CD4/CD8. The standard ratio is about 1 to 1.5. If the disease is advancing, CD4 will reduce and CD8 will increase or stay the same and the CD4/CD8 ratio will be <1, indicating disease progression.

2.9. HIV Cellular Immune Responses:

After infection within the early weeks, acute viremia is related with CD8 T cell activation: the amount of CD8 T cells increases up to 20-fold above the normal range, whereas CD4 T cell numbers decrease rapidly. Cells with CD4 receptors at the location of HIV entry become infected and viral multiplication start inside them. The infected cells would release virions by surface budding or infected cells can undergo lysis to discharge new virions, which would then infect extra cells. Certain virions of HIV are carried from the place of infection to the regional lymph nodes where further immune system cells become infected. Large quantities of virus become stuck here in complexes of specific cells called follicular dendritic cells (FDCs) *(Mechanism of CD4 T- cell depletion, 2005).*CD4+ T cells, the principal targets of HIV, is infected as they meet HIV confined on FDCs by other immune system cells through CD4 molecules on their

surfaces *(Mechanism of CD4 T- cell depletion, 2005).* Macrophages and monocytes may keep large numbers of the virus without being destroyed. CD4+T cells are vital reservoirs of HIV. Regular immune processes can trigger these cells leading to the production of new HIV virions. Increased cytokines production in and around germinal centres such as tumour necrosis factor (TNF) and IL- 6 can activate CD4+ T lymphocytes and make them extra vulnerable to HIV infection *(Mechanism of CD4 T- cell depletion, 2005).* Stimulation permits cells which have not been infected to be more simply infected and increases multiplication of HIV in earlier cells infected to be extra infected and increases replication of HIV in previous cell. After infection, CD4+ T cells may leave the germinal centre and infect other CD4+ T cells that assemble in the region of the lymph node surrounding the germinal centre *(Mechanism of CD4 T- cell depletion, 2005).*

Numerous concepts of how HIV may destroy or incapacitate CD4+ T cells in an HIV infected person have been proposed and include:

-Direct cell killed. Infected CD4+ T cells may be killed directly when large quantities of virus are made and bud off from the cell surface, disrupting the cell membrane, or when viral proteins and nucleic acids are produce inside the cell, interfering with cellular mechanism *(Mechanism of CD4 T- cell depletion, 2005).*

- Syncytia formation. Cells which are infected may fuse with nearby uninfected cells through CD4 – facilitated fusion, making syncytia. The death of uninfected cells has been linked with this mechanism of cell to cell spread of HIV infection *(Mechanism of CD4 T- cell depletion, 2005.)*

3. Apoptosis. Cellular regulation distortion may lead to the killing of infected CD4+ T cells by HIV proteins, leading to their death by a process known as programmed cell death or apoptosis. Cells which are not infected may also experience apoptosis. Investigation have revealed in cell cultures that the HIV envelope alone or bound to antibodies sends an incorrect signal to CD8+ T cells causing them to go through apoptosis even though not infected by HIV *(Mechanism of CD4 T- cell depletion, 2005).*

2.10. HIV Humoral Responses (Production of antibodies against HIV)

In the course of HIV infection anti-HIV antibodies start to develop 4 to 8 weeks later. Antibodies are primarily focussed against cell-free virions, even though specific

antibodies might also destroy HIV-infected cells. Antibodies are primed to identify specific genetic variants of HIV

2.11. HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN MANAGEMENT OF HIV AND AIDS.

HAART is a combination therapy aimed at suppressing human immunodeficiency virus replication to undetectable levels and sustaining this suppression for months or years in a considerable number of persons *(Definition of HAART, 2005).* With the awareness, in the early 1980's that acquired immunodeficiency syndrome was caused by a retrovirus; further research was carried on to get effective antiviral agents to tackle this devastating disease. Active research efforts have been aimed at development of drugs that interfere with the viral live cycle. HAART has proved to be effective in decreasing plasma viral RNA to undetectable levels in most treated patients. No drug however, has resulted in cure of HIV. HAART has remarkably reduced the rate of death in patients with HIV type 1. HAART has changed AIDS from a deadly disease into a possibly treatable and chronic form *(International Journal of Public Health, 2002).* Although about 90 % of HIV infected persons live in the developing world, less than 5% of those who need ART in the developing world, get it *(Quality Technical Bulletin on HIV/AIDS-STI in Ghana, 2003).*

UNAIDS projected that a total of 2.5 million mortalities have been prevented in developing and middle -income countries since 1995 due to the roll out of antiretroviral drug*(UNAIDS,2011).*

The therapy package involves the use of antiretroviral drugs that attack the virus itself with other non-Antiretroviral drugs such as Co-trimoxazole to avert and treat opportunistic infections (OIs) that occurs when the immune system is compromised by HIV *(Reviewed by Gilks C et al, 2006).* Examples of this opportunistic infections are Mycobacterium Avium Complex (MAC) disease, Pneumocystis carinii pneumonia and Cytomegalovirus (CMV) retinitis which are common to HIV type-1. These medications have caused a decline in opportunistic infection more than 75% in the USA and Europe *(Reviewed by Kaplan, Hanson et al, 2000)*. Individuals are helped to deal with emotional and traumatizing consequences through counseling and support mechanisms as well as to enable one to accept to live with a disabling, possibly incurable disease. The degree to which HAART increases longevity shows that, persons diagnosed with AIDS in 2003 and who received treatment would survive, on average, 14 more years

than if they had not been treated at all *(Reviewed by Maria and Soriano, 2006).* Highly active antiretroviral therapy also decreases the chances of transmitting HIV from one person to the other through sex, though the risk of spread is not entirely eliminated. HAART use amongst infected-HIV persons has been associated with a 60% decrease in transmission risk behavior in multiple locations *(See Bunnel and Cherutich, 2008).*

HAART coverage increase from 7% in 2003 to 42% in 2008, with particularly high expansion attained in eastern and southern Africa (48%) *(UNICEF, 2009).* Estimates from UNAIDS and WHO shows that, the projected 14.2 million HIV persons, 47% (6.6 million) qualified for medication in developing and middle-income countries were taking life-saving HAART in 2010, a rise of 1.35 million since 2009 *(UNICEF, 2009).* There are more than 35 different antiretroviral drugs approved by Food and Drugs Agency (FDA).These antivirals which are now being in used are grouped into six classes to treat HIV infections *(Reviewed by Granich, R. M., Gilks, et al, 2009).* All of the six classes attack HIV in a different ways as indicated in their mechanism of action.

2.12 CLASSES OF HAART AND THEIR MECHANISM OF ACTION

2.12.1 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs/NtRTI).

These drugs have been the first agents available for the treatment of HIV infection. Even though less effective against HIV type 1 compared to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs). It was approved in 1987

8 drugs make up the Nucleoside/Nucleotide Reverse Transcriptase Inhibitors class; these are Lamivudine (3TC, Epivir), Zidovudine (ZDV, Retrovir) formerly azidothymidine (AZT), Abacavir (ABC, Ziagen), Emtricitabine (FTC, Emtriva), Didanosine (ddI, Videx), Tenofovir (TDF, Viread), Stavudine (d4T, Zerit), Zalcitabine (ddC, Hivid).

5 out of these drugs are available in Ghana and these are Zidovudine, Lamivudine, Abacavir, Emtricitabine and Tenofovir. Tenofovir is a Nucleotide Reverse Transcriptase Inhibitor (NtRTI) *(Reviewed by Piliero PJ, 2004).*

2.12.2. Mechanism of Action

Inhibit reverse transcription through fusing into the newly produced viral DNA and preventing its further elongation.

2.12.3. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

It was in 1996 that Non-Nucleoside reverse transcriptase inhibitors (NNRTIs) were introduced with the approval of Nevirapine. These medications prevent effective action against HIV type-1 and are part of the favourite first routines *(See Shen L, et al, 2008).* Particularly, Efavirenz, is the most important inhibition of viral infectivity among these antiretroviral drugs *(Reviewed by Shen L, et al, 2008).* Efavirenz (Sustiva), (Rescriptor), Nevirapine (Viramune) and Delavirdine are the firstgeneration NNRTIs. Etravirine (Intelence) and Ripivirine (Edurant) are the secondgeneration NNRTIs in which Etravirine (Intelence) was permitted for use in USA in 2008, whiles Ripivirine (Edurant) was permitted in 2011 (*FDA, Approves new HIV treatment, 2011)*. Nevirapine (NVP) and Efavirenz (EFV) are the NNRTIs used in Ghana

All NNRTIs show similar mechanism of action. Efavirenz and Nevirapine which are first generation drugs share related resistance patterns, whiles Etravirine and Ripivirine been second generation drugs display a more unique resistance profile *(Rimsky LT, et al, 2009).*

2.12.4. Mechanism of Action

Prevent reverse transcriptase directly by binding to the enzyme and interfering with its function.

2.12.5. Fusion or Entry Inhibitors

The first class of ART drugs to target the HIV replication cycle extracellularly was fusion inhibitors (FIs).It was consented to be in use 2003. The exceptional mechanism of action gives extra alternatives for drugs in persons who are highly treatment resistant. The use of these drugs has been restricted, due to the production costs and time, inadequate coverage from insurance establishments, HIV drug-assistance programme, difficult administration (hypodermic injection) and adverse drug effects.

The only product sold in this class is Enfuvirtide (Fuzeon).

2.12.6. Mechanism of Action

Prevent HIV from binding to or entering human immune cells

2.12.7. Chemokine Receptor Antagonists

Maraviroc (Selzentry) was permitted in August 2007 by the FDA to be used and has been the first drug in an original class of ART representatives named chemokine receptor 5 (CCR5) antagonists. It links the fusion inhibitors (FIs) as additional category of representative below the broad ART treatment class of HIV entry inhibitors.

2.12.8. Mechanism of Action

Prevent CCR5 and CXCR4 which are receptors found on CD4 used by HIV1 to attached itself to CD4 for entry or fusion.

2.12.9. Intergrase Inhibitors

The Intergrase inhibitors are made up of Raltegravir (Isentress) accepted for use in 2007 as the first Intergrase inhibitor medication. In treatment of HIV type 1 Dolutegravir (Tivicay) is used in amalgamation with additional ART for elderly and teenagers above 12years with a body weight of at least 40kg. This ART was approved to be used in August 2013 by FDA and this is an Intergrase strand transfer inhibitor (INSTI). Elvitegravir (Cobiostat) is another medication of Intergrase inhibitor *(See DeJesus E, et al, 2006).*

2.12.10. Mechanism of Action

Inhibit Intergrase enzyme needed by HIV to insert its genetic component into human cells.

2.12.11. Protease Inhibitors

These were introduced in 1995 and are an important part of regimen of HIV infection *(DHHS, Antiretroviral guidelines for Adults and Adolescents, 2011).* 8 drugs have been agreed for use, and these are

Tipranavir (Aptivus), Saquinavir (Invirase),

Fosamprenavir (Lexiva), Atazanavir (Reyataz), Darunavir (Prezista).

Nelfinavir (Viracept), Indinavir (Crixivan), Lopinavir/Ritonavir (Kaletra).

But in Ghana, two of these drugs are recommended for use. These are Ritonavir boosted Atazanavir (ATV/r) and Ritonavir boosted Lopinavir (LPV/r). Though all protease inhibitors show the same mechanism of action, they have essential variances in pharmacokinetics, efficiency, and adverse effects.

2.12.12. Mechanism of Action

This attack viral assembly by preventing protease enzymes used by HIV to split budding proteins for concluding assembly of new virions.

Accessible in most countries whereas the rest are accessible in resource rich countries *(WHO Guide Report: 6. 2013).*

2.13. HAART-related adverse effects

Although the use of HAART medications has a deep influence on the AIDS epidemic in the world, it should be understood that the therapy carries their own disadvantages. There is an increase of adverse effects due to HAART ranging from mild to severe which have been well documented in many studies and this are a major safety concern *(Reviewed by Hawkins,2010).* Every drug in the highly active antiretroviral combination has its own range of side effects and it is not likely to predict how an HIV patient will be affected by the drug therapy even though some common side effects are known during pre-marketing clinical trials. The three common adverse effects of HIV medications are nausea, diarrhea and fatigue *(Reviewed by Emery et al., 2008).* Less recurrent abnormalities like lactic acidosis with hepatic steatosis, progressive rising neuromuscular weakness and longer term complications for example dyslipidemia and fat mal-distribution were not known up until after the medication had been in use for years *(See Hawkins, 2010).*

Highly active antiretroviral therapy adverse-effects may be transient or may continue throughout medication and are among the most primary reasons for changing or suspending medication as well as for medication non-adherence *(See Hawkins, 2010).* Drug side effects perform a key role in determining adherence to highly active antiretroviral therapy and it is perhaps the most important factor of a regimen's success *(Reviewed by d'Arminio et al., 2000).* In unusual cases, some drug-associated adverse effects may result in major illness and even death. HAART drug abnormality affecting the haematological and biochemical parameters are monitored after every six months *(See Sullivan, T. M., Strachan et al, 2007)* but it is symptom directed in most less resources areas. Variations in relation to severity of adverse effects of HAART may be determined by individual differences, age, region, ethnicity and interaction with other drugs, including alcohol and type or class of drug *(See Dieterich et al., 2002).*

HAART can have a wide range of side effects which are expediently recognized by class of offending agent used and classified as short and long-term abnormalities *(Reviewed by Hawkins, 2010).* The main adverse effects for each antiretroviral class used in HAART are summarized in Table 2.1 below.

Table 2.1: Side effects related to different classes of HAART

HAART Class	**Examples of drugs**	**Adverse effects**	
		Short term effects	**Long term effects**
NRTIs	Zidovudine, Stavudine, Didanosine	Anemia, nausea, lactic acidosis, pancreatitis, rash, myopathy and Nausea.	Dyslipidemia, lipoatrophy, hepatic steatosis, heart disease, hepatotoxicity, Renal insufficiency and bone loss
NNRTIs	Efavirenz, Nevirapine, Etravirine	Rash and Hypersensitivity reaction.	CNS disorders, hepatotoxicity, teratogenicity, and hypertriglyceridemia
PIs	Atazanavir, Indinavir, Lopinavir	Nausea, diarrhea, nephrolithiasis, rash, and Jaundice.	Dyslipidemia, insulin resistance, hepatotoxicity, and Heart disease

NRTIs- Nucleoside reverse transcriptase inhibitors; NNRTsI- Non-nucleoside reverse transcriptase inhibitors and PI – Protease inhibitors. ***Source: Hawkins, 2010***

2.14. THE RECOMMENDED ANTIRETROVIRAL REGIMEN IN GHANA

In Ghana, three antiretroviral drugs namely Protease Inhibitors (Pls), Non- Nucleoside Reverse Transcriptase Inhibitors (NNRTI's) and Reverse Transcriptase Inhibitors (NRTI's) are uses as HAART which serves as a standard antiretroviral (ARV) routine for management of HIV positive patients. Usage is a combined two Nucleoside Reverse Transcriptase Inhibitors (NRTI's) and effective Protease Inhibitors (PI) or Non -Nucleoside Reverse Transcriptase. *(Reviewed by Montessori et al., 2004)*

2.15. HAART RELATED HAEMATOLOGICAL ABNORMALITIES.

Haematological abnormalities are normally the greatest common appearance of advance HIV infection and AIDS *(Reviewed by Erhabor et al, 2006).* These toxicities may possibly happen due to the infection of HIV itself, HIV related opportunistic infections, malignancies or the highly active antiretroviral therapies *(See Evans et al, 2000).*

2.15.1 Anaemia

Fisch bach et al, 2009 considered a person to be anaemic when the haemoglobin value for male is less than 13g/dl and female less than 12g/dl and this is evaluated by measuring the haemoglobin concentration (Hb) in the blood.

Levine et al, 2000 study shows that anaemia is predominant in infected HIV persons, happening in almost 30% of those with asymptomatic infection of HIV and in 75% to 80% of patients with clinical AIDS.

A study which was carried out in a Port Harcourt University Teaching Hospital for 100 ART naïve patients had a mean haemoglobin of 10.25+/-1.97g/dl (range 6.3114.2g/dl), with severe anaemia occurring in 80% of patients while 20% were non anaemic *(See Erhabor, Ejelle et al, 2005).* Current studies show that as HIV/AIDS disease progresses, the anaemia prevalence and severity also increases.

A cohort longitudinal studies conducted among HIV naïve patients shows that anaemia was 18% in asymptomatic seropositive patients, symptomatic middle stage HIV disease was 50% and Center for Disease control defined AIDS was 75% *(See Spivak & Barnes et al, 1989*).

Another study conducted by *Zon ET & Groopman JE, 1988* on HAART naïve patients shows that 8% of asymptomatic HIV patients were anaemic, 20% of symptomatic middle stage HIV patients were anaemic and 71% of HIV patients were anaemic based on Center for Disease Control (CDC) defined AIDS.

Highly active antiretroviral therapies can also induce anaemia among HIV patients taken the ART. A study done by *Fischl, et al, 1990* shows HIV patients on Zidovudine experiences haematological abnormalities such as anaemia and neutropenia. This haematological abnormalities is as a result of Zidovudine being myelosuppresive to the red blood cells originators in the bone marrow *(See De Jesus et al, 2004). Carr and Cooper* study shows that about 5%-10% of most persons taken Zidovudine normally developed anaemia within the first three months of drug.

A trial study by *Waller et al, 1988* shows that about 31% of HIV patients on Zidovudine required red blood cell transfusion whiles receiving the therapy. Another study done by *Torpey et al, 2003* in the St. Martins Deporees Hospital at Akwatia and Atua Government Hospital in the Manya Krobo District in line with anaemia of HIV patients taking ART in Ghana shows that 74.2% of the patients on Zidovudine were anaemic with their haemoglobin concentration less than 11g/dl. Patients on Delavirdine also reported an adverse effect of anaemia *(Cohen & Sande et al, 1999).*

2.15.2. Leucopenia

Cheesbrough, 2005 define leucopenia as the decline in the number of total white blood cells count below what is normal for a person's age, gender, and physiological condition. This is usually seen in untreated HIV patients at a high percentage especially with patients with deeper immunodeficiency *(Sande et al, 1999).* Study conducted by *Zon and Groopman* shows low leucopenia counts in asymptomatic HIV persons at 13% and 44% of leucopenia with HIV patients defined in line with Center for Disease Control for AIDS.

Sande et al, 1999 Cohort multicenter AIDS study shows that HIV positive persons who have average CD4+T-lymphocyte counts greater than 700 cells/mm^3 was 0.8% which had unusually low WBC counts, whiles leucopenia was found in HIV patients with average CD4+ T-lymphocyte counts fewer than 249 cells/mm^3 of 13.4% of the patients.

2.15.3. HAART-Induced leucopenia

The greatest predominant cause of low WBC counts in HIV patients is ART. Zidovudine drug has a myelosuppresive effects on the HIV patients. A study done by *Hawkins &Gold et al, 1986* shows that leucopenia (<500 cells/mm^3) advanced in 16% of Zidovudine treated patients in the original placebo controlled study of Zidovudine therapy for progressive HIV disease and indicative middle-stage HIV disease. 2% of placebo treated patients became leucopenia to this degree.

2.15.4. Lymphopenia

The main target of HIV is the CD4+ T cells. These cells are damaged once the cells are affected. There is decrease in the CD4+ counts as the disease progresses. Lymphopenia

is symptomatically produced in HIV infections where CD4+ level can be used as an indicator of HIV infection.

2.15.5. The response of CD4+ T- cell in HAART.

About 20-30% of HIV patients have discordant result (*Journal of infectious diseases, 2002),* either with reduction in viral load, without a suitable CD4 response or with an increase CD4 in spite of a poor virologic response *(JAMA, 2001).* Between HIV patients starting highly active antiretroviral therapy, *Huang et al,2000,* indicated a significant increase in WBC, platelets and neutrophils with CD4+T cells as plasma HIV RNA levels decrease, *Isgro et al,2000,* recognised an increase in bone marrow mononuclear cells as well as functional development in progenitor and stem cells evaluates *(Isgro, Mezzaroma et al, 2000).* The reason for the improvements is most probable due to the reversal of inhibitory effects of HIV replication, but statistics by *Sloand & Young, 2000,* shows that the Protease Inhibitors HIV may have a direct effect on hematopoietic cells *(Reviewed by Sloand, Kumar et al, 2000).* It was indicated that inhibition of caspase-1 by the protease inhibitor, Ritonavir, causing a decrease in apoptotic rate and increase colony forming ability of bone marrow cells obtained from infected HIV persons. Hence, ART may have additional effect improving their key role in suppressing viral replication.

2.15.6. Thrombopenia

Thrombopenia is defined as disorder in which there is an abnormally low amount of thrombocytes as a result of immune system malfunction *(Reviewed by McMillan et al, 2007).*

Platelets are made by megakaryocytes cells in the bone marrow and are necessary to help blood clot. Anytime a blood vessel is damaged and begins leaking blood, the odd shaped and sticky platelets clump together to plug the leak and prevent on-going blood loss.

The number of thrombocytes can be low for many causes in HIV infection: Bone marrow cells may produce less thrombocytes either because they are directly infected by HIV or inhibited by abnormal immune responses, such as the development of antibodies against platelet a disorder called Immune Thrombocytopenic Purpura (ITP). The antibodies are known as autoantibodies, as they attack itself and signal the spleen to damage and excrete the thrombocytes from the body.

Ballem et al 1992, stated that both thrombocytes existence, thrombocytes production is declined in HIV-associated thrombocytopenia. This study together with the in vitro result that HIV can infect megakaryocytes, propose that HIV infection of megakaryocytes may be a direct cause of thrombocytopenia.

A cohort study by *Soland, Klein et al, 1992* shows 4% prevalence of thrombocytopenia in 1004 symptomatic infected HIV patients.

A study in Nigeria Port Harcourt, shows that 100 HIV patients gave a mean thrombocytes count of $170.07\pm49.03x10^9$/L, thrombocytopenia happened in 10% of the HIV patients *(Reviewed by Erhabor, Ejelle et al, 2005).*

A study in United Kingdom, London, reported thrombocytes of less than 150,000 cells/mm^3in 30% of persons with advance disease of HIV and lymphadenopathy was 8% among patients (See *Spivak et al, 1989).*

2.15.7. Thrombopenia Induced by ART

Certain HAART used for the treatment of HIV/AIDS can occasionally destroy the bone marrow. Example certain Nucleoside Reverse Transcriptase Inhibitors can result in reduction of thrombocytes production. These NRTIs include, Zidovudine, Lamivudine and Abacavir *(Definition of Thrombocytopenia, 2005).*

Production of thrombocytes from the bone marrow is also most often reduced by certain ART. Ganciclovir (Cymevene), Valganciclovir (Valcyte), Indinavir (Crixivan), are drugs which can induce thrombocytopenia. Other drugs such as Cotrimoxazole and Hydroxycarbamide (Hydrea) which can also induce thrombocytopenia are used for the treatment of opportunistic infections such as Mycobacterium avium intracellular (MAI), cytomegalovirus (CMV) and tuberculosis.

Drugs like Ribavirin and α-interferon meant for the treatment of hepatitis C virus can likewise cause thrombocytopenia.

A study Reviewed by *Miquez et al, 2002* shows that thrombocytopenia existed in 70% which is high among 37 individuals most of them were taking highly active antiretroviral therapy, at two years follow up.

Carbonara, 2001 shows a retrospective study of 15 individuals with related severe thrombocytopenia who started highly active antiretroviral therapy.

2.15.8. HAART- RELATED BIOCHEMICAL ABNORMALITIES.

2.15.9. HAART-related Liver abnormalities and its diagnostic biomarkers

The liver and the kidney plays some important roles in the human system. The vital role played by the liver is, it converts and clear chemicals such as drugs. It can also be susceptible to damage from toxicity of these drugs. Owing to its exceptional metabolic rate and close by association with the gastrointestinal tract, blood coming right from gastrointestinal organs and then spleen through portal veins is received by the liver. These drugs and xenobiotic are transport in near-undiluted form *(See Larry et al., 2004).* Certain HAART agents when taken over long term or short term, may injure the liver leading to hepatotoxicity *(Reviewed by Sulkowski, 2004).* During a conference by the National Institutes of Health of USA a finding was presented on liver toxicity and its retrospective analysis indicated that hepatotoxicity is related to b all classes of antiretroviral drugs in use *(See Clifford et al., 2003).* All antiretroviral drugs can induce hepatotoxicity which is described by elevation of ALT/AST levels to at least two times the upper limit of normal (ULN) can happen per drugs from the classes *(Reviewed by Sulkowski et al., 2000).* HAART-induced hepatotoxicity may be asymptomatic on HIV patients, but this hepatic damage can be diagnosed during routine blood investigation. Other patients also develop symptoms comprising fatigue, nausea jaundice and itching *(See O'Brien et al., 2003)*. The variability studies among the standards of classifying the severity of hepatotoxicity is broad. Transaminases above normal limits among HIV-patients at baseline are considered to develop hepatotoxicity. That is when ALT or AST increase above the upper limits of normal range *(MoH, 2007).*

To detect the presence of liver disease, liver function tests (LFTs) are performed to differentiate between different types of liver complications, and scale the degree of recognized liver injury and response to medication. Liver function tests are a group of chemical pathology laboratory blood tests designed to give information about the state of a patient's liver *(Reviewed by Abrescia et al., 2005).* Liver functionalities are related to Liver function tests and examples are Albumin (ALB) and total proteins (PROT), and this are determined using the liver biomarkers. Hepatocellular integrity is associated with aminotransferases (ALT and AST) and some are related to cholestasis - biliary tract blockage- example gamma-glutamyl transferase (ɣ -GT) and alkaline phosphatase (ALP) *(MoH, 2007).* The two liver indicators useful in the monitoring, assessment and management of patients with hepatic dysfunction due to drug toxicity are ALT and ALP. Classes of patients at higher risk for drug-induced hepatotoxicity include: Obese individuals, females' old patients, viral sicknesses and pre-existing liver

disease *(See Wit et al., 2002).* The most essential biochemical parameters of the liver significant in diagnosing drug-hepatotoxicity are Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Albumin (ALB), Total protein (PROT), Alkaline phosphatase (ALP), Total bilirubin, Direct bilirubin,

Gamma glutamyl transferase (γ-GT).

2.15.10. HAART-related Renal abnormalities and their diagnostic biomarkers

Metabolism and excretion of waste products of metabolism comprising drug metabolites is one of the major role of the kidney. The ability of the kidneys to function appropriately is affected negatively by HIV infection and some HIV drugs may also harm the kidneys *(Reviewed by Pataki, 2006)* making it susceptible to various types of kidney damage comprising disturbances of fluid and electrolyte metabolism and instabilities in acid-base balance. Highly active antiretroviral therapy can cause various renal syndromes clinically, as well as, various electrolyte and acidbase complications, chronic kidney disease, acute renal injury (ARI) and lactic acidosis *(Rao, 2001)*. These injuries happen through multiple mechanisms, including allergic reactions and precipitation of undissolvable drug crystals within renal tubular lumens and direct tubular toxicity, *(See Wyatt et al., 2009)*. Kidney toxicities comprising acute renal injury (ARI), chronic kidney disease (CKD), end-stage renal disease and tubulopathies are some of the adverse side-effects of antiretroviral therapy requiring renal replacement therapy *(See Ogundahunsi et al., 2008).*Kidney destruction manifests itself as proximal tubular injury with related reduction in glomerular filtration and patients often develop, glycosuria, increased serum creatinine and low serum phosphate tubular proteinuria, *(Reviewed by Thompson, 2011).*Kidney disease has been linked mainly with tenofovir ever since the parent Nucleotide Reverse Transcriptase Inhibitor tenofovir is vigorously gathered in the proximal renal tubule through the activity of kidney-specific organic anion transporters 1 *(See Cihlar et al., 2001).* Buildup of the therapy in kidney proximal tubules as a result of a likely disproportion in the acceptance and efflux has been associated in drug-induced Fanconi syndrome *(Reviewed by Izzedine et al., 2005).*

Fanconi syndrome causes acute proximal tubular dysfunction and has been reported in individual s receiving tenofovir and adefovir, most frequently in patients with poorly controlled HIV disease, causing elevated creatinine *(Reviewed by Eaton, 2005).* Diagnosis of HAART induced side effects on the kidney encompass performing full

Kidney function tests (KFTs), a group of chemical pathology laboratory blood tests considered to give evidence about the state of a patient's kidney *(See Daugas et al., 2005).* Indirect kidney markers specifically serum creatinine (CREAT) and blood urea nitrogen (BUN), plus electrolytes; sodium (SOD), potassium (K^+) and chloride (CL^-) are tests to determine kidney function The degree of renal dysfunction is determined by measuring serum creatinine levels or creatinine clearance/glomerular filtration rate (GFR).The gauge of renal dysfunction (insufficiency) is graded as mild, moderate or severe based on the GFR or serum creatinine level as outlined in Table 2.2.

Table 2.2: Grading of renal dysfunction

Grade of Severity of Renal dysfunction	Glomerular Filtration Rate (ml/minute)	Serum Creatinine (umol/L)
Normal	>50	<160
Mild	20-50	160-300
Moderate	10-20	300-450
Severe	<10	>450

Source*: MoH, 2007.*

Another predictive biomarker for renal disease is an elevated level of protein in the urine, a condition we refer to as proteinuria. It is a qualitative test that shows positive when there is existence of albumin in urine which shows injury to renal glomeruli owing to viral infection or highly antiretroviral therapy toxicities among other causes. The practical significance of kidney biochemical biomarkers and their levels are important in diagnosing kidney-toxicity. The most essential biochemical parameters of the kidney significant in diagnosing drug-kidney abnormalities are Blood Urea

Nitrogen (BUN), Creatinine (CREAT), Sodium (Na), Potassium (K), Chloride (Cl^-)

CHAPTER THREE

METHODOLOGY

3.0. SAMPLE SIZE

This was determined using the sample size calculator by means of Rao soft, Inc a single population formula considering the following: The standard score for the confidence interval of 95% level, Margin of error 5%, Response Distribution of 50%, Population size=559,548 which represent population and housing census data of 2010 in Sekondi Takoradi Metropolis.

The Sample Size (N) 200 correspondents will be representative for the study using the sample size calculator from Rao soft considering the assumption above.

(Rao soft Inc., 2004).

3.1. STUDY DESIGN

Comparative cross-sectional study of a sample size of 200 correspondents who were tested positive for HIV (HIV1 or HIV2) at the EffiaNkwanta HIV/AIDS unit within the period of 10 months (March-December). Samples were taken and analysed for the baseline parameters (Pre-HAART) to check for haematological, biochemical abnormalities and for viral loads. Samples were taken again after 6 months (Post-HAART) to check for haematological, biochemical abnormalities and for viral loads responses.

3.2. ETHICAL CONSIDERATION

Ethical Consideration was sought from the Committee on Human Research, Publications and Ethics, Kwame Nkrumah University of Science and Technology and School of Medical Sciences.

3.3. INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria for enrolment of the total respondents were stated as follows:

- The age of the HIV patients must be 13 years and above.
- Have confirmed laboratory proof of HIV infection.

- Have history of taking no previous highly active antiretroviral therapy (HAART naive).
- Agree to take HAART drug,

Exclusion criteria were as follows;

- Those with recent blood transfusion.
- Pregnant women were excluded from the research study.

3.4. QUESTIONNAIRE AND DATA COLLECTION

A structured questionnaire was filled by each patient to obtain their socio demographic data such as Age, Sex, and etc. Clinical history during the research study at the hospital

3.5. LABORATORY TECHNIQUES

3.5.1. Haematological Parameters:

Haematological parameters made up of Total white blood cells count (WBC), Red blood cells count (RBC), Haemoglobin (Hb), Platelet count (PLT), Absolute white blood cell were determined using Automated Sysmex *XS-1000i/XS-500i* haematology analyser.

3.5.2. Principles of Procedure

The Sysmex XS *(XS-100i/ XS-500i)* is an Automated Haematology Analyser intended for in vitro diagnostic use in screening patient populations found in clinical laboratory. The *Sysmex XS-1000i and SX- 500i* can analyse and output the results of 24 for Europe and 21 for America's biomarkers of a blood sample. The Sysmex XS1000i and XS-500i perform analysis of WBC and differential with semiconductor laser. The RBC's and platelets are analysed by the RBC detector using the Hydro Dynamic Focusing method. Data analyse is displayed on the information Processing Unit (IPU). Haemoglobin (HGB) is analysed by the HGB detector based on the SLS haemoglobin detection method. The XS-1000i/XS-500i main unit measures and controls samples whiles Information Processing Unit (IPU) processes data generated by the measuring device. (Appendix III).

3.5.3. Biochemical Parameters

Biochemical parameters were determined using the serum of the HIV/AIDS patients to look for the following serum enzymes: Albumin (ALB), ALT, AST, ALP Creatinine (CRbi), Total Protein (PRTB), Urea (URSL), using an Automated Selectra ProS chemistry analyser.

3.5.4. Principles of Procedure

The Selectra ProS is an automated chemistry analyser which run assays on clinical samples and is used in combination with reagents for in vitro diagnostic measurement of analytes. Samples of blood serum, plasma, urine, cerebrospinal fluid and aqueous standard solutions to detect the presence of analytes relating to disease or drugs. Analytes commonly includes enzymes, substrates, electrolytes, specific proteins, drugs of abuse. The results then gives clinicians' feedback on toxicology and on renal, cardiac and liver function.

The Selectra ProS has been designed as a table-top system with all standard and optional components fitted in one unit. The Selectra ProS standard components are: Cuvette rotor, Pipettor arm, Combined sample and reagent rotor, Lamp unit (inside cabinet), Cooling unit (inside cabinet), Touch panel PC running the analyser software, Water/waste containers (inside cabinet), Dry ISE unit (inside cabinet), Syringes (inside cabinet/probe).

Samples are loaded into the machine and tests are programme by the user. A probe measures an aliquot of samples and places it into a reaction vessel. Reagents are added from an on board refrigerated supply. Incubation time is allowed, if required; then photometric or ion-selective electrode (ISE) testing determines the concentration of analyte. Results are displayed on screen or sent to a printer or computer. (Appendix III).

3.5.5. Viral Load Assay

Viral loads of the HIV/AIDS type 1 patient's plasma were measured. Using an Automated measured COBAS AmpliPrep/ COBAS TaqMan HIV-1 Qual Test.

3.5.6. Principles of Procedure

The COBAS AmpliPrep/COBAS TaqMan HIV-1 Qual test is a qualitative or quantitative nucleic acid amplification test used for the detection of Human Immunodeficiency Virus Type 1 (HIV-1) RNA and proviral DNA in plasma, anticoagulated fresh whole blood and dried blood spots (DBS). This test uses the COBAS AmpliPrep instrument for automated sample processing and the COBAS TaqMan Analyser or COBAS TaqMan 48 Analyser for automated amplification and detection.

The COBAS AmpliPrep/COBAS TaqMan HIV-1 Qual Test is based on four major processes: 1. Sample pre extraction and incubation. 2. Sample preparation to isolate HIV-1 target nucleic acids; 3. Reverse transcription of the target RNA to generate complementary DNA (cDNA), and 4. Simultaneous amplification of target cDNA or proviral DNA by Polymerase Chain Reaction (PCR) and detection of cleaved duallabelled oligonucleotide detection probe specific to the target.

The COBAS AmpliPrep/COBAS TaqMan HIV-1 Qual Test is used with EDTA plasma, fresh EDTA anticoagulated whole blood and dried blood spot (DBS) punches as sample types. These sample types require a manual, pre-analytical sample pre – extraction. This step is executed by the use of a separate reagent kit, the Specimen Pre-Extraction Reagent, consisting of a lysis reagent.

The COBAS AmpliPrep/COBAS TaqMan HIV-1 Qual Test allow automated sample preparation followed by automated reverse transcriptase, PCR amplification and detection of HIV-1 target RNA or proviral DNA and HIV-1 internal Control (IC) Armored RNA. The Master Mix reagent contains primers and probes specific for either HIV-1 target RNA or proviral DNA and HIV-1 IC RNA. The detection of amplified DNA is performed using target-specific and IC- specific dual-labelled oligonucleotide probes that permit independent identification of HIV-1 target amplicon and HIV-1 IC amplicon. (Appendix III).

3.6. STATISTICAL ANALYSIS

Data for haematological and biochemical Assays collected were entered into Microsoft excel database, checked and corrected for data entry errors. It was then transported into SPSS. Paired sample t-test and one-way ANOVA were used for the statistical analysis.

CHAPTER FOUR

4.0. RESULTS

Among the 200 participants recruited for this study, 156(78%) were females. Majority of the study population (95.5%) were infected with HIV type 1. More than half of the study respondent reported being in a stable married, however 27% of the respondent were divorced. At the time of this study 44.5% of the study respondents had attained at least middle leaver or junior high leaver of study. Most of the study respondents were classified as coming from a low economic background with monthly earnings ranging from 50 to 500 Ghana cedis (See Table 4.1).

Table 4.1: Socio-demographic characteristic of the population under study

Parameter	Total	Male	Female
Total Respondent	200(100)	44(22.00)	156(78.00)
Age 20-29 30-39 40-49	41.36±11.36 30 (15) 60 (30) 58 (29)	41.57±10.3	41.29±11.67
50-59 60-69 >70	36 (18) 12 (6) 8 (4)		
HIV 1	191(95.50)	42(21.00)	149(74.50)
HIV 2	9(4.50)	2(1.00)	7(3.50)
Marital Status			
Married	107(53.50)	29(14.50)	78(39.00)
Single	39(19.50)	9(4.50)	30(15.00)
Divorce	54(27.00)	6(13.64)	48(24.00)
Highest Education			
None	33(16.50)	2(1.00)	31(15.50)
Primary	34(17.00)	3(1.50)	31(15.50)
Middle/JHS	89(44.50)	22(11.00)	67(33.50)
Technical/SHS	30(15.00)	11(5.50)	19(9.50)
Tertiary	14(7.00)	6(3.00)	8(4.00)
Economic Status			
Low	164(82.00)	25(12.50)	139(69.50)
Medium	36(18.00)	19(9.50)	17(8.50)

Data is presented as figure with percentage in parenthesis, mean ± Standard deviation.

Among the haematological indices evaluated in this study, an average significant increase in red blood cell count and haemoglobin level was recorded after six (6) months of HAART therapy. Significant reduction in lymphocytes count was also seen post- HAART therapy.

For the biochemical indices assayed in this study no significant change was observed in AST. The Total Protein and Albumin levels were found to have elevated significantly after HAART therapy. Significantly, the levels of Alanine transaminase (ALT) elevated which is a key surrogate biomarker for diagnosing cellular hepatoxicity. After treatment, Serum Alkaline Phosphatase (ALP) significantly increased. This is a key surrogate index for diagnosing cholestasis. Serum Urea and Serum Creatinine significantly also elevated after treatment. Urea and Creatinine are the biomarkers used for diagnosing renal disorders. The prevalence of these abnormal liver enzymes (ALT and ALP) (p- 0.0456, p- 0.0392) and kidney enzymes (Creatinine and Urea) (p-0.0117, p- 0.0407) are the important markers for diagnosing drug-induced toxicities affecting the liver and the kidney. As seen from Table 4, the average viral load significantly reduced from 137966.30±4.05 (copies/ml) to 2037.49±22.86 (copies/ml) (p- <0.0001) after treatment (See Table 4.2).

Table 4.2: Haematological, biochemical and viral indices of HIV patients before and after treatment

Parameter	Pre- HAART	Post-HAART	p-value
Haematological Indices			
RBC ($x10^6$cell/µl)	3.99±1.38	4.36±1.31	0.0001
Haemoglobin (g/dl)	11.91±3.75	12.94±3.84	0.0001
WBC ($x10^9$cell/L)	4.90±1.57	4.97±1.45	0.6819
Neutrophil ($x10^9$cell/L)	2.20±0.85	2.01±0.82	0.1034
Lymphocytes ($x10^9$cell/L)	2.36±0.97	1.97±0.56	0.0001
Platelets ($x10^9$cell/L)	180.57±1.88	188.86±1.76	0.1118
Biochemical Indices			
Total Protein (g/L)	89.27±17.5	96.72±14.13	<0.0001
Albumin (g/L)	38.76±1.58	43.66±1.35	0.0002
AST (U/L)	30.13±1.77	30.41±1.77	0.7962
ALT(U/L)	24.19±1.83	26.46±1.85	0.0456
ALP(U/L)	224.48±135.53	268.15±142.63	0.0392

Urea (mmol/L)	3.24±0.54	3.56±0.72	0.0117
Creatinine(umol/L)	80.04±29.07	83.49±32.06	0.0407
Viral Indices			
Viral Load (copies/ml)	137966.30±4.05	2037.49±22.86	<0.0001

Data is presented as mean±Standard deviation. p. is significant at 0.05.

Units of the various Biomarkers analyze and its Reference ranges:

RBC-Red Blood Cell [($x10^6$cell/µl),(4.20-6.30)] Haemoglobin [(g/dl),Male-(13.0-18.0) Female-(12.0-16.5)] [WBC-White Blood Cell [($x10^9$cell/L),(2.50-8.50)] Neutrophil [($x10^9$cell/L),(4.00-7.50)] Lymphocytes [($x10^9$cell/L),(2.0-4.0)] Platelets [($x10^9$cell/L),(140-440)] AST- Aspartate transaminase [(U/L) (0.0-40.00)] ALT- Alanine transaminase [(U/L) (0.040.0)] Urea[(mmol/L),(2.10-7.10)] Creatinine[(umol/L),(71.0-115.0)] ALP-Alkaline Phosphatase [(U/L),(0.0-270)] Total Protein [(g/L),(60.0-83.0)] Albumin [(g/L),(35.0-52.0)].

Among the male participants, Red blood cell count, Total Protein, Albumin, Alkaline Phosphatase, and Alanine transaminase (ALT) levels, Serum Urea and Serum Creatinine significantly increased after HAART therapy. No significant changes were observed for Haemoglobin, White blood cell count, Neutrophil count, lymphocyte count, platelet count, Aspartate transaminase (AST). The male study population presented with a significant reduction in viral load after therapy.

On the average significant increased levels were found among the female participants for Red blood cell count, Haemoglobin, Total Protein, Alkaline Phosphatase level, Alanine transaminase (ALT) levels, Albumin, Serum Urea and Serum Creatinine, after HAART therapy. No significant changes were recorded for White blood cell count, Neutrophil count, lymphocyte count, platelet count, Aspartate transaminase (AST). A significant reduction in viral load after HAART therapy was also recorded among the female study participants See Table 4.3.

Table 4.3: Haematological, biochemical and viral indices of HIV patients before and after treatment stratified by gender

Parameter	Male(44)			Female(156)		
	Pre- HAART	Post-HAART	p-value	Pre- HAART	Post-HAART	p-value
RBC	4.05±1.51	4.60±1.27	0.0085	3.98±1.34	4.30±1.32	0.0019
Haemoglobin	12.65±4.18	13.17±3.87	0.4087	11.70±3.61	12.88±3.84	0.0001
WBC	4.41±1.6	4.78±1.44	0.2624	5.04±1.56	5.02±1.45	0.9192
Neutrophil	2.08±0.91	1.92±0.83	0.4768	2.24±0.93	2.04±0.83	0.1447
Lymphocytes	2.02±0.17	1.86±0.75	0.4547	2.47±0.9	2.01±0.5	0.0001
Platelets	172.39±1.88	188.63±1.71	0.1030	182.94±1.88	188.93±1.78	0.3264
Total Protein	93.86±15.03	100.45±14.32	0.0018	87.98±17.97	95.67±13.94	<0.0001
Albumin	43.31±1.39	48.87±1.33	0.0266	38.60±1.63	43.88±1.35	0.0014
AST	34.85±1.67	39.84±1.56	0.0743	28.91±1.79	28.18±1.79	0.5431
ALT	27.39±1.78	37.08±1.66	0.0004	23.35±1.83	24.03±1.84	0.0177
ALP	179.57±1.74	197.41±1.31	0.0493	156.25±1.17	163.51±1.72	0.0361
Urea	3.72±0.57	4.21±1.07	0.0243	3.12±0.52	3.39±1.06	0.0429
Creatinine	106.34±33.89	115.45±34.18	0.0839	72.62±22.69	74.48±24.98	0.0394
Viral Load	176441.20±3.65	2641.19±24.17	<0.0001	128558.26±4.16	1891.47±22.73	<0.0001

Data is presented as mean±Standard deviation. p is significant at 0.05.

Units of the various Biomarkers analyze and its Reference ranges:

RBC-Red Blood Cell [($x10^6$cell/µl),(4.20-6.30)] Haemoglobin [(g/dl),Male-(13.0-18.0) Female-(12.0-16.5)] [WBC-White Blood Cell [($x10^9$cell/L),(2.50-8.50)] Neutrophil [

($x10^9$cell/L),(4.00-7.50)] Lymphocytes [($x10^9$cell/L),(2.0-4.0)] Platelets [($x10^9$cell/L),(140-440)] AST- Aspartate transaminase [(U/L) (0.0-40.00)] ALT- Alanine transaminase [(U/L) (0.0-40.0)] Urea[(mmol/L),(2.10-7.10)] Creatinine[(umol/L),(71.0-115.0)] ALP-Alkaline Phosphatase [(U/L),(0.0-270)] Total Protein [(g/L),(60.0-83.0)] Albumin [(g/L),(35.0-52.0)].

Among the haematological biomarkers evaluated in this study, based on percentage number of subjects with cytopenias, 95(47.5%) mild anaemia whiles 10(5%) for severe anaemia for pre-HAART. For post-HAART, mild anaemia was 64(32%) whiles 45(22.5%) for severe. Mild lymphopenia was 29(14.5%) whiles 19 (9.5%) for severe lymphopenia for post-HAART. Post- HAART had mild anaemia as 64(32%) and 45(22.5) for severe anaemia. Mild lymphopenia was 37(18.5%), whiles 8(4%) for severe lymphopenia for post-HAART as seen in Table 4.4.

Table 4.4: Using haematological biomarkers to assess varying degree of Cytopenias (Abnormalities) in HIV Patients in percentage.

	Cytopenias	Anaemia	Leucopoenia	Neutropenia	Lymphopenia	Thrombopenia
Pre-HAART	Mild	95(47.5%)	10 (5 %)	45 (22.5%)	37 (18.5 %)	14 (7 %)
	Moderate	40(20%)	8(4 %)	24 (12 %)	22 (11 %)	20 (10 %)
	Severe	45(22.5%)	8 (4 %)	76 (38 %)	19 (9.5 %)	11 (5.5 %)
Post - HAART	Mild	64(32%)	7 (3.5%)	52 (26%)	29 (14.5%)	11 (5.5%)
	Moderate	32 (16%)	3 (1.5%)	26 (13%)	20 (10%)	18 (%)
	Severe	10.5%)	3(1.5%)	89 (44.5%)	16 (8%)	8 (4%)

Data is presented as figure with percentage in parenthesis

Table 4.5: Using haematological biomarkers to assess varying degree of Cytopenias (Abnormalities) in HIV Patients in terms of gender.

	Cytopenias	Anaemia	Leucopoenia	Neutropenia	Lymphopenia	Thrombopenia
Pre-HAART Male	Mild	23(11.5%)	2(1%)	11(5.5%)	8(4%)	5(2.5%)
	Moderate	6(3%)	3(1.5%)	4(2%)	4(2%)	6(3%)
	Severe	3(1.5%)	3(1.5%)	18(9%)	8(4%)	3(1.5%)
Pre -HAART Female	Mild	60(30%)	5(2.5%)	35(17.5%)	20(10%)	13(6.5%)
	Moderate	43(21.5)	4(2%)	15(7.5%)	20(10%)	15(7.5%)
	Severe	8(4%)	5(2.5%)	62(31%)	12(6%)	8(4%)
Post-HAART Male	Mild	20(10%)	2(1%)	18(9%)	10(5%)	1(0.5%)
	Moderate	5(2.5%)	3(1.5%)	6(3%)	5(2.5%)	5(2.5%)
	Severe	1(0.5%)	1(0.5%)	16(8%)	4(2%)	3(1.5%)
Post-HAART Female	Mild	56(28%)	5(2.5%)	49(24.5%)	33(16.5%)	19(9.5%)
	Moderate	22(11%)	4(2%)	27(13.5%)	23(11.5%)	12(6%)
	Severe	4(2%)	2(1%)	73(36.5%)	9(4.5%)	6(3%)

Data is presented as figure with percentage in parenthesis.

Keys

Cytopenias	**Mild**	**Moderate**	**Severe**
Anaemia [Hb (g/dl)]	10.1-11.9	8.0 – 10.0	< 8.0
Leucopoenia [WBC x 10^9/L]	2.5 – 2.9	2.1 – 2.5	<2.0
Neutropenia (Absolute neutrophils counts x10^9/L)	3.9 – 2.5	2.4 – 2.2	<2.0
Lymphopenia	1.9 – 1.5	1.4 – 1.0	<1.0
Thrombopenia (platelets (x 10^9/L)	101 - 139	50 - 100	<50

References range

Haemoglobin concentration (Hb g/dl) 13.0-18 for males, 12 – 16.5 for females

White blood cell count (WBC x 10^9/L) 2.6 – 8.3)

Neutrophils (Absolute neutrophils counts (Neut x10^9/L) 2.30 – 7.5)

Lymphopenia (Absolute Lymphocytes counts

Thrombopenia (platelets counts (PLT x 10^3 140.0 – 4400)

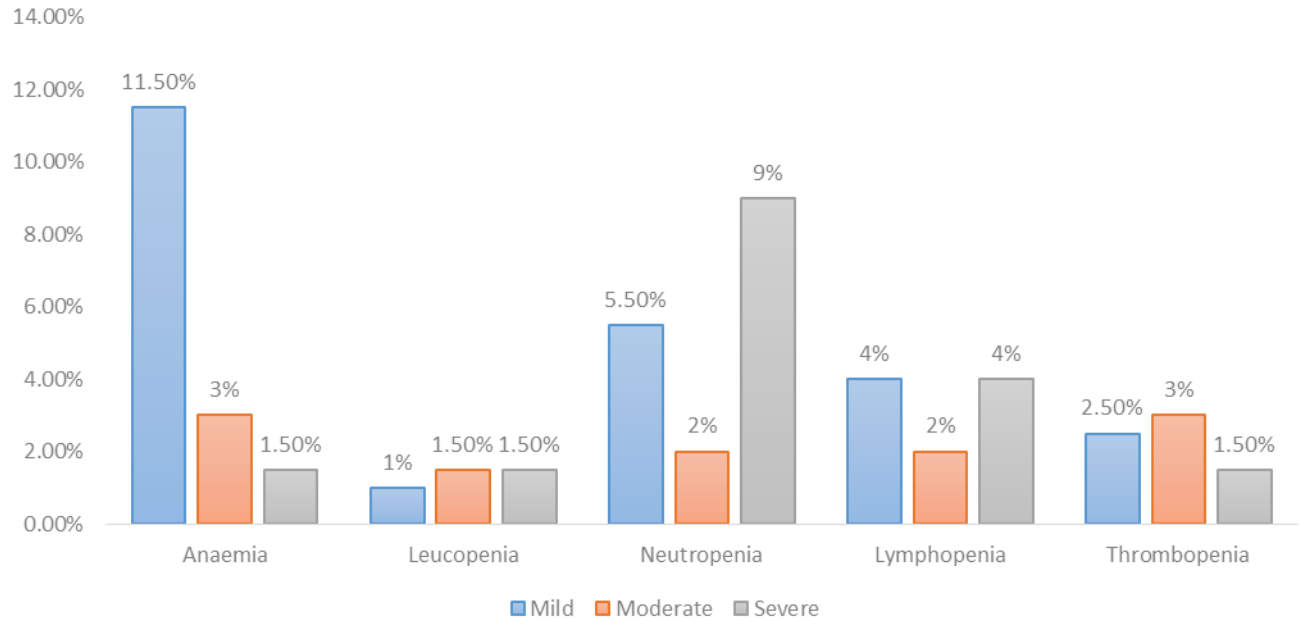


Figure 4.1: A graph showing variations in haematological biomarkers due to Cytopenias (Abnormalities) in Pre-HAART male HIV patients.

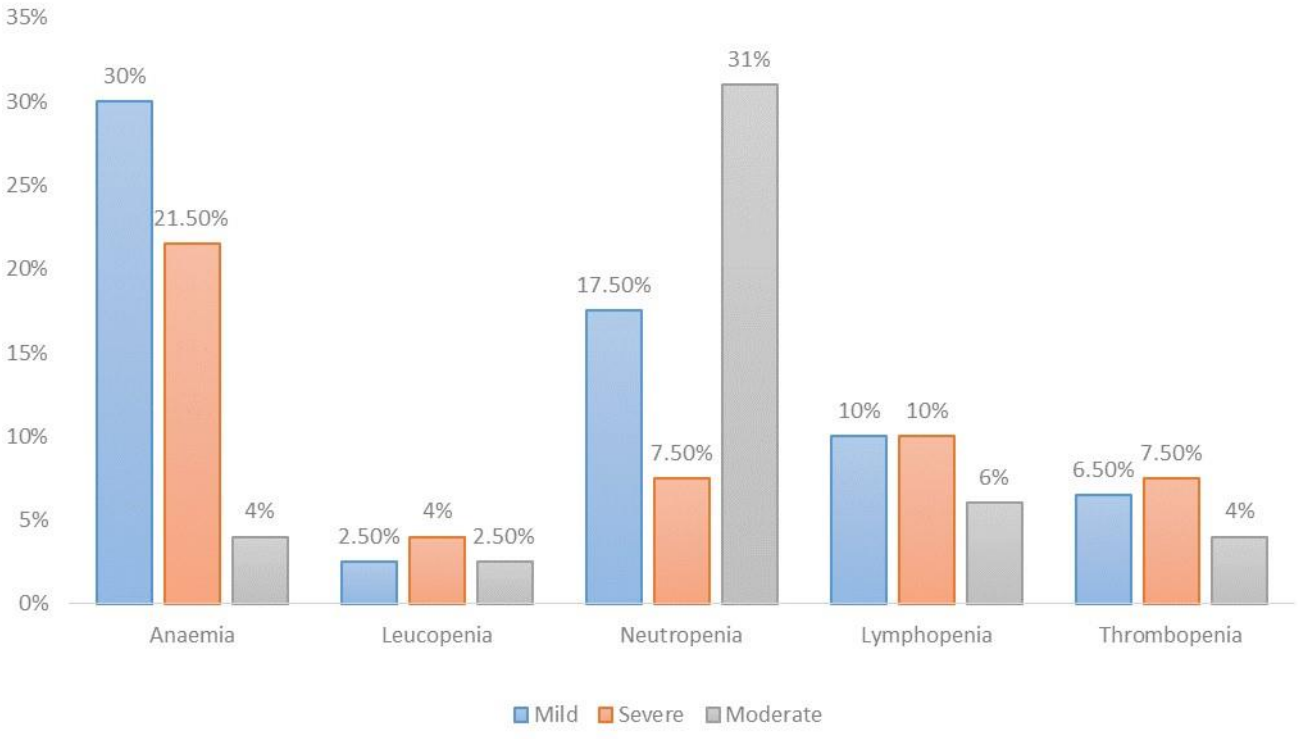


Figure 4.2: A graph showing varying degree in haematological biomarkers due to

Cytopenias (Abnormalities) in Pre-HAART female HIV patients

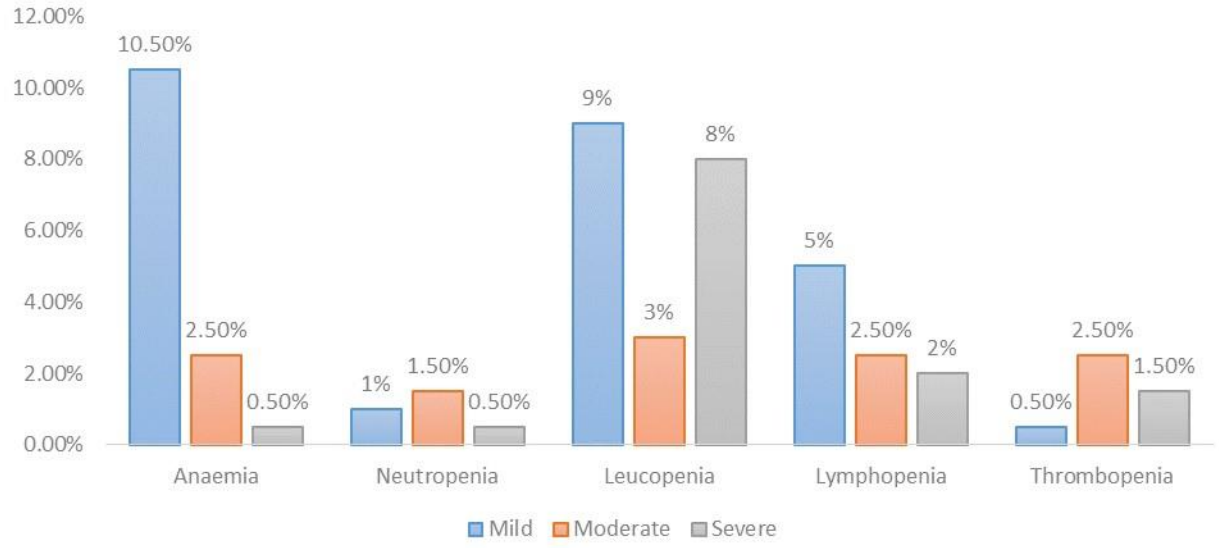


Figure 4.3: A graph showing differences in haematological biomarkers due to Cytopenias (Abnormalities) in Post-HAART male HIV patients

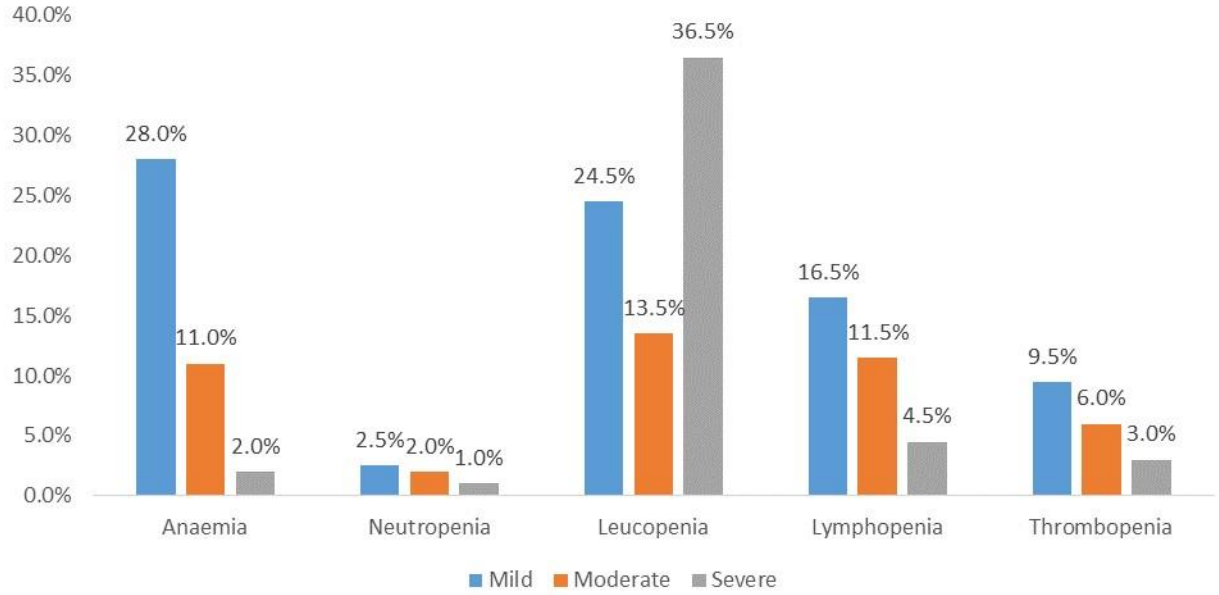


Figure 4.4 a graph showing variation in haematological biomarkers due to Cytopenias (Abnormalities) in Post-HAART female HIV patients.

As seen from Table 8, depending on the equation used to estimate the glomerular filtration rate, renal insufficiency (chronic kidney disease) ranged from 19(9.50%) to 36(18.00%) pre HAART therapy to 20(10.00%) to 33(16.50%) six months' post HAART therapy. Serum creatinine levels or creatinine clearance/glomerular filtration rate (GFR) is measured to determine degree of kidney dysfunction as a result of HIV infection or HAART medications. Grade of Severity of Renal dysfunction and it

Glomerular Filtration Rate in ml/minute: Normal (stage1) = >50, Mild (stage3) =20-50, Moderate (stage4) =10-20, Severe (Stage5) =<10. See Table 4.6 below.

Table 4.6: Chronic kidney disease prevalence among HIV seropositive before and after treatment

Parameter	**4v-MDRD**		**CKD-EPI**	
	Pre- HAART	Post-HAART	Pre- HAART	Post-HAART
Stage 1 (≥ 90)	123(61.50)	116(58.00)	53(26.50)	59(29.50)
Stage 2 (60 to 89)	58(29.00)	64(32.00)	111(55.50)	108(54.00)
Stage 3 (20 to 50)	19(9.50)	19(9.50)	33(16.50)	30(15.00)
Stage 4 (10 to 20)	0(0.00)	1(0.50)	3(1.50)	1(0.50)
Stage 5 (<10)	0(0.00)	0(0.00)	0(0.00)	2(1.00)
CKD (Stage 3+4+5)	**19(9.50)**	**20(10.00)**	**36(18.00)**	**33(16.50)**

Data is presented as figure with corresponding percentage in parenthesis. 4v-MDRD – Four variable Modification of Diet in Renal Disease, CKD-EPI – Chronic Kidney Disease Epidemiology collaboration.

Table 4.7: Effect of treatment combination on mean viral load, haemoglobin, total protein and serum albumin of HAART patients.

Panel	Viral load log (copies/ml)	Haemoglobin(g/dl)	Total Protein (g/l)	Albumin (g/l)
1	3.15	12.80	99.68	1.64
2	2.79	14.20	94.27	1.75
3	3.46	11.83	99.45	1.67
4	3.45	13.66	93.52	1.61
5	2.88	13.32	95.51	1.68
Eta square (n^2)	**0.028**	**0.048**	**0.041**	**0.070**
P – value (p)	**0.3982**	**0.0482**	**0.0833**	**0.0058**

HAART effect on viral load, haemoglobin, total protein and serum albumin levels. P value is significant at < 0.05. (η_2)-Eta square for effect size: $\eta^2 \leq 0.04$ – Weak effect, $0.04 < \eta_2 \leq 0.36$ moderate effect, $\eta^2 > 0.36$ strong effect. Treatment Panel 1- (Lamivudine/ Zidovudine/ Efavirenz), **Panel 2** (Emtricitabine/ Tenofovir/ Efavirenz), **Panel 3** (Lamivudine/ Zidovudine/ Nevirapine), **Panel 4** (Lamivudine /Efavirenz/Tenofovir) and **Panel 5** (Emtricitabine/ Tenofovir/ Nevirapine).

After HAART experience no significant difference in log mean viral load emerged among the participants on the different treatment panels (p-0.3920), though participants on treatment panel 2-(Emtricitabine/ Tenofovir/ Efavirenz) reported the lowest mean viraemia (2.79 copies/ml) and those on treatment panel 3-(Lamivudine/ Zidovudine/ Nevirapine) the highest (3.46 copies/ml). The different treatment panel had a **weak effect** on the level of viraemia (**η^2 -0.028)**

After HAART experience significant difference in haemoglobin levels was recorded among the participants on the different treatment panels (p-0.0482). Participants on treatment panel 3-(Lamivudine/ Zidovudine/ Nevirapine) reported the lowest mean haemoglobin level (11.83 g/dl) and those on treatment panel 2-(Emtricitabine/ Tenofovir/ Efavirenz) presented the highest average haemoglobin (14.20 g/dl). Different panel of

HAART treatment was found to have a **moderate effect** on the levels of haemoglobin (**η^2 - 0.048)**

As seen in the treatment panel participant were put on, there was no significant difference after treatment in the average levels of total protein among the groups (p- 0.0833) Participants on treatment panel 4-(Lamivudine /Efavirenz/Tenofovir) presented the lowest mean serum total protein (93.52g/l) and those on treatment panel1(Lamivudine/Zidovudine/Efavirenz) presented the highest mean serum total protein. (99.68g/l). The different treatment panel had a **weak effect** at the end of treatment differences of total protein level among the groups (**η^2 -0.041)**.

After HAART experience significant difference in serum Albumin levels was recorded among the participants on the different treatment panels (p-0.0058). Participants on treatment panel 4-(Lamivudine /Efavirenz/Tenofovir), reported the lowest average serum Albumin level (1.61 g/l) and those on treatment panel 2-(Emtricitabine/ Tenofovir/ Efavirenz) presented the highest average serum Albumin (1.75 g/l). Different panel of HAART treatment was found to have a **moderate** effect on the levels of serum Albumin (**η^2** - 0.07). See Table 4.7 above.

CHAPTER FIVE

DISCUSSION

Retroviral infections are life-threatening in developing countries, affecting the socioeconomic status of individuals, families, communities and the entire society *(Ibeh et al., 2013).* The number of reported cases of HIV infections is observed to be higher in the female sex than in the male counterpart *(Denue et al., 2013; Ibeh et al., 2013*). In the current study, among the 200 participants who were recruited, majority were females 156 (78%), infected with HIV-1 (95.5%), as well as attained at least middle or junior high level education (44.5%) with low economic background. The current findings are consistent with findings reported previously among HIV infected individuals on HAART and HAART naïve patients in various populations *(Denue et al., 2013; Ibeh et al., 2013; Venkataramana, 2013; Bello et al., 2014; Enawgaw et al., 2014*). Among factors thought to be driving the gender difference in favour of women with respect to the risk of HIV include early start of sexual activity, sexually transmitted diseases, broader surface area of the vagina and longer semen-vaginal contact, low levels of education, occupation as well as standard of living which may be a reflection of an increase in commercial sex workers *(Obirikorang et al., 2014*). In Ghana, the practice of female genital mutilation is still prevalent and this could be contributing to the high incidence of sexually-transmitted infections including HIV among women. Majority of males in this part of the world are circumcised and male circumcision gives some degree of protection, therefore, the risk of infection is minimized 8-fold over uncircumcised men *(C.J. Miller, J.R. McGhee et al, 1993).*

It is believed that single or unmarried individuals are more likely to acquire HIV infection than married partners *(Ibeh et al., 2013).* Contrary to the results of this study, a greater number of retroviral positive participants recorded a stable union (53.5%) compared to single or unmarried individuals. This observation also agrees with earlier findings of

Enawgaw et al. (2014) and Denue et al. (2013). In an attempt to explain the association of high HIV prevalence with married partners, Haque and Soonthorndhada (2009) posited previously that there is high awareness of STI risk and condom use among unmarried individuals compared to their married counterparts. The study also reported the lowest age group of HIV patients was above 70 years of age at 8(4%) whiles the highest age group of HIV patients were between the ages 30-39 years at 60(30%).This work is in line with a study done by *Amornkul & Vandenhoudt et al, 2009* which shows that top most age peak which are sexually active and predispose to HIV infection fell within this age bracket of 30-34 years.

HIV-1 infection alone or in combination with HAART therapy, has been shown to influence haematological parameters including blood haemoglobin levels, leukocyte count, erythrocyte sedimentation rate and absolute eosinophilic count *(Ramana and Rao, 2013).* Among the haematological parameters evaluated in this study, an average significant increase in red blood cell count and haemoglobin level was recorded after six (6) months of HAART therapy. Significant reduction in lymphocytes count was also seen post-HAART therapy. A study carried out in Nigeria to determine the biochemical and haematological changes in HIV subjects receiving Winniecure antiretroviral drug recorded significant increases in haemoglobin levels and packed cell volume estimations but a significant drop in absolute lymphocyte count from the first visit through to the third visit of 6 weeks intervals (*Ibeh et al., 2013).* Similarly, a comparative crosssectional study at the antiretroviral clinic of the Gondar University Hospital, Northwestern Ethiopia reported a significantly higher levels of haemoglobin, red blood cell counts with significantly low white blood cell counts in patients on HAART therapy in comparison to treatment naïve patients *(Enawgaw et al., 2014).* Though it remains unclear the actual mechanism explaining lower haemoglobin levels and other red cell indices at baseline compared to those on treatment, *Debasu et al., (2015)* suggested that

HIV is thromboembolic and cytotoxic, dysregulating β lymphocytes thereby altering the release of cytokines which down-regulates growth of bone marrow progenitors leading to anaemia.

Among the male participant, Red blood cell count mean increase significantly (p-0.0085) but there were no significant changes in haemoglobin (p-0.4087), implying that the HAART medication may not be the cause of the increase in haemoglobin in the male HIV patients. Significant increase on mean was found among the female participants 'with regard to Red cell count and haemoglobin (p-0019, p-0.0001) after HAART. Therefore, pre-HAART patients in both sexes have a high risk of developing anaemia as a result of under production of erythropoietin due to the HIV infection *(Zon et al, 1988).*

Anaemia is predominant in HIV infected individuals. The calculated prevalence of anaemia pre-HAART mild, moderate, and severe anaemia were 95(47.5%), 40(20%) 45(22.5%) and 64(32%), 32(16%), 10(5%) post-HAART which indicates a significant reduction of anaemia after HAART.This could be as a result of immune restoration, reduction in viral loads after HAART and combination of ART has had a positive effect in regulating anaemia in some HIV positive patients. This finding is in line with a study by *Levine et al, 2004,* which indicates that the use of highly active antiretroviral therapy in anaemic patients correlate with improvement in haemoglobin concentration over a period. These study is also in sharp contrast with a study done by *Torpey et al, 2003* at St. Martin's hospital at Akwatia and Atua Government hospital which indicated that 74.2% of HIV persons on Zidovudine were anaemic with their haemoglobin concentration less than 11g/dl.

The occurrence of anaemia among sex as in, Figure 4.1-4.4 shows a higher percentage of females being more anaemic as compare to their male counterpart in pre and post HAART respectively. *Volberding, 2004* credited it to menstruation because of the blood loss in

women during that period and the loss of iron stores that occur with pregnancy and delivery. *Levine et al, 2004* made a similar finding in their study and credited it to sex and race. But this finding differs from a study conducted by *Omoregie et al, 2009,* which reported a high prevalence of anaemia in male pre- HAART patients compared to their female counterparts. This is also in contrast with a work done by *DeJesus et al, 2004*.

There was an average increase in WBC but not statistically significant post HAART (p0.6819). With respect to gender, there was an increase in WBC which was also not statistically significant (p-0.2624, p-0.9192). This may imply that the HAART drug may not be the cause of the increase in WBC in HIV patients but rather the elevation of WBC may indicate infection, lack of response to treatment or an abnormality.

The prevalence increase in leucopenia among HIV patients may cause a decreases in CD4 counts and this may be due to suppression of bone marrow and direct infection of T cell. This condition decreases the body's resistance to numerous opportunistic infections and the patients becomes more vulnerable to bacterial infections and requires medical care, the disorder may become life-threatening *(Akinbami et al, 2010)*. But this study shows stages of leucopenia prevalence of 10(5%) mild, 8(4%) moderate and 8(4%) severe pre-HAART as compare to 7(3.5%), 3(1.5%), and 3(1.5%) post-HAART.This reduction of leucopenia from pre-medication to post-HAART may be as a result of suppressive activity of the antiretroviral drug on the virus response and suppression of opportunistic diseases. This work is consistent with a study done in Nigeria by *Erhabor et al, 2006* which found a higher percentage of leucopenia on pre-HAART patients due to myelosuppression by HIV itself and opportunistic diseases. The prevalence of leucopenia was higher in female as compared to their male counterpart. These may be due to the fact that HIV infected females will probably have a faster progression in the depletion of WBC than infected males.

Biochemical abnormalities are among the main clinicopathological outcomes of HIV patients on ART *(Ibeh et al., 2013)*. Hepatotoxicity or hepatocellular damage may be

marked by elevations in liver enzymes due to drug interactions and are significant complications in HIV patients on HAART *(Khan et al., 2014).* It is estimated that, 14%20% of patients will experience elevation of liver enzymes after being put on antiretroviral therapy *(García-Samaniego et al., 2001).* There was significant increase in the levels of ALT and ALP after treatment. The results notwithstanding, indicate an association of hepatocellular injury with HAART treatment in participants with retroviral infection. The findings concur with those obtained by *Ngala et al. (2015)* among Ghanaian HAART-experienced individuals for at least 1-6 months and *Bello et al. (2014)* among HIV/AIDS patients on HAART for 2-8 years in the Nigerian population. The transaminases are enzymes known to be associated with hepatocytes which are poured into circulation when the liver cells are attacked by the virus or the antiretroviral agent *(Ngala et al., 2015).*

Glomerular filtration rate (GFR) was measured to determine degree of renal dysfunction and the prevalence of chronic kidney disease among HIV seropositive before and after medication. Renal insufficiency has been identified in about 30% of HIV infected patients with profound impact on people of African descent *(Owiredu et al., 2013).*

There was a reduction in renal dysfunction from 18% to 16.5% post HAART when CKD-EPI equation was used hence, the findings suggest that renal pathology appeared to have improved among these individuals after antiretroviral treatment using the CKD-EPI score. This observation contrasts with findings from related studies conducted in the Ghanaian population where there was a worsening of renal function among HAART experienced individuals compared to their HIV positive HAART naïve counterparts *(Owiredu et al., 2013; Obirikorang et al., 2014).* This prevalence rate of chronic renal disease among pre-HAART patients may be attributed to HIV replication effects of the virus on the kidney.

The goal of viral load measurement is to monitor clinical status and treatment response in patients with HIV infection *(Bouza et al., 2009).* In the present study, the average viral

load significantly reduced from 137966.30±4.05 (copies/ml) to 2037.49±22.86 (copies/ml) after treatment. Similarly, among the male and female subpopulations, there was a significant reduction in viral load after HAART therapy, [176441.20±3.65 vs 2641.19±24.17 and 128558.26±4.16 vs 1891.47±22.73] (copies/ml) respectively. This is in concordance with results reported among participants enrolled in the Nutrition for Healthy Living Study in Boston and Rhode Island as well as in the Spanish HIV population *(Mwamburi et al., 2005; Bouza et al., 2009)*. This study is also consistent with a findings reported by *TS LI R, Tubiana, et al,1998* were HAART decreases viral load levels and increases CD4 T-cell counts in patients with advance HIV-1 infection Essentially, the combination antiretroviral therapy employs at least three antiretroviral agents directed against at least two distinct molecular targets and is the underlying basis for preventing drug resistance *(Arts and Hazuda, 2012).* The action of combination therapy serves to suppress viral replication, reduce plasma HIV-1 viral load to undetectable levels resulting in a significant reconstitution of the immune system which is reflected in the increase in circulating CD4+ T-lymphocytes *(Arts and Hazuda, 2012).*

5.6. LIMITATIONS

- Cluster of Differentiation test (CD4) could not be done to know the immunological status and HAART response of the HIV/AIDS patients.

5.7. FINDINGS

- Although HAART may have toxicity effect on haematological biomarkers, the study shows a decrease in haematological cytopenias post-HAART as compare to pre-HAART.
- There was also a reduction in renal damage post-HAART as compare to pre-

HAART.

- Viraemia levels were reduce post-HAART.

5.8. CONCLUSION

HAART therefore, had a positive impact on haematological, biochemical enzymes and viral load levels as compare to HIV infection. Henceforth, healthcare providers should give much attention to HIV/ AIDS patients taking highly active antiretroviral therapy so that toxicity effects that may arise as a result of intake of ART can be reduce to improve the quality of life and decrease the risk of mortality. Also, there should be harmonization of highly active antiretroviral therapy regimen and dosage prescription in order to reduce abnormalities levels.

5.9. RECOMMENDATION

- CD4 test must be done so that immunological status of the HIV/AIDS patients can be determined.
- More health education should be encourage so that HIV/AIDS patients would understand the need for them to take their HAART regimen.

REFERENCES

Abrescia, N., D'Abbraccio, M., Figoni, M., Busto, A., Maddaloni, A., & Marco, M. D. (2005). Hepatotoxicity of antiretroviral drugs. *Current pharmaceutical design*, *11*(28), 3697-3710.

Adediran, I. A., & Durosinmi, M. A. (2006). Peripheral blood and bone marrow changes in patients with acquired immunodeficiency syndrome. *African journal of medicine and medical sciences*, *35*, 85-91.

Akinbami, A., Oshinaike, O., Adeyemo, T., Adediran, A., Dosunmu, O., Dada, M. ... & Vincent, O. (2010). Hematologic abnormalities in treatment-naive HIV patients. *Infectious Diseases: Research and Treatment*, *3*, 45.

Andersen. CL, Tesfa D, Siersma VD et al, 2016; 279 (6): 566 prevalence and clinical significance of neutropenia discovered in routine complete blood cell counts: a longitudinal study.

Andersen, C. L., Tesfa, D., Siersma, V. D., Sandholdt, H., Hasselbalch, H., Bjerrum, O. W., ... & Palmblad, J. (2016). Prevalence and clinical significance of neutropenia discovered in routine complete blood cell counts: a longitudinal study. *Journal of internal medicine*.

Arts, E. J., & Hazuda, D. J. (2012). HIV-1 antiretroviral drug therapy. *Cold Spring Harbor perspectives in medicine*, *2*(4), a007161.

Attili, S. V. S., Singh, V. P., Rai, M., Varma, D. V., Gulati, A. K., & Sundar, S. (2008). Hematological profile of HIV patients in relation to immune status-a hospitalbased cohort from Varanasi, North India. *Turk J Hematol*, *25*, 13-19.

Avery L.B., Zarr M.A., Bakshi R.P., Siliciano R.F. and Hendrix C.W. (2013) Increasing extracellular protein Bello S.I., Onunu A.N. and Erah P.O. (2014). Long-term effect of Haart on biochemical profiles of HIV/AIDS patients in a tertiary health facility in Benin city,Nigeria. *Tropical Journal of Pharmaceutical Research* 13(11), 1941-1946.

Ballem, P. J., Belzberg, A., Devine, D. V., Lyster, D., Spruston, B., Chambers, H., ... & Mikulash, K. (1992). Kinetic studies of the mechanism of thrombocytopenia in patients with human immunodeficiency virus infection. *New England Journal of Medicine*, *327*(25), 1779-1784.

Belperio, P. S., & Rhew, D. C. (2004). Prevalence and outcomes of anemia in individuals with human immunodeficiency virus: a systematic review of the literature. *The American journal of medicine*, *116*(7), 27-43.

Bisaso, K. R., Owen, J. S., Ojara, F. W., Namuwenge, P. M., Mugisha, A., Mbuagbaw, L., ... & Mukonzo, J. K. (2014). Characterizing plasma albumin concentration changes in TB/HIV patients on anti-retroviral and anti–tuberculosis therapy. *In silico pharmacology*, *2*(1), 1.

Boffito, M., Back, D. J., Blaschke, T. F., Rowland, M., Bertz, R. J., Gerber, J. G., & Miller, V. (2003). Protein binding in antiretroviral therapies. *AIDS research and human retroviruses*, *19*(9), 825-835.

Bouza, J. M. E., Padilla, E. S., Alcalde, F. J. L., González, B. N., Rello, S. R., Herrero, J. A., & de Lejarazu Leonardo, R. O. (2009). Viral Load in Spanish HIV patients: trends since the introduction of HAART. *Revista Española de Quimioterapia*, *22*(1), 34-37.

Brookmeyer, R. (1991). Reconstruction and future trends of the AIDS epidemic in the United States. Science 253:37-42.

Bradley, H., Hall, H. I., Wolitski, R. J., Van Handel, M. M., Stone, A. E., LaFlam, M., ... & Patel, R. (2014). Vital signs: HIV diagnosis, care, and treatment among persons living with HIV—United States, 2011. *MMWR Morb Mortal Wkly Rep*, *63*(47), 1113-7.

Brodt, H. R., Kamps, B. S., Gute, P., Knupp, B., Staszewski, S., & Helm, E. B. (1997). Changing incidence of AIDS‐defining illnesses in the era of antiretroviral combination therapy. *Aids*, *11*(14), 1731-1738.

Bunnell, R., & Cherutich, P. (2008). Universal HIV testing and counselling in Africa. *The Lancet*, *371*(9631), 2148-2150.

Cameron, D. W., D'Costa, L., Maitha, G., Cheang, M., Piot, P., Simonsen, J. N. ... & Plummer, F. (1989). Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *The Lancet*, *334*(8660), 403407.

Carbonara, S., Fiorentino, G., Serio, G., Maggi, P., Ingravallo, G., Monno, L. ... & Angarano, G. (2001). Response of severe HIV-associated thrombocytopenia to highly active antiretroviral therapy including protease inhibitors. *Journal of Infection*, *42*(4), 251-256.

Carr, A., & Cooper, D. A. (2000). Adverse effects of antiretroviral therapy. *The Lancet*, *356*(9239), 1423-1430.

Centers for Disease Control and Prevention (CDC. (2005). HIV prevalence, unrecognized infection, and HIV testing among men who have sex with men-five US cities, June 2004-April 2005. *MMWR. Morbidity and mortality weekly report*, *54*(24), 597.

Centers for Disease Control and Prevention (CDC. (2011). Characteristics associated with HIV infection among heterosexuals in urban areas with high AIDS prevalence---24 cities, United States, 2006-2007. *MMWR. Morbidity and mortality weekly report*, *60*(31), 1045.

Centers for Disease Control and Prevention. (2011). Risk, Prevention, and Testing Behaviors Related to HIV and Hepatitis Infections—National HIV Behavioral Surveillance System: Injecting Drug Users, May 2005-February 2006. HIV Special Surveillance Report 7. *HIV Special Surveillance Report*, *7*.

Centers for Disease Control and Prevention. HIV Testing Trends in the United States, 2000-2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; January 2013.

Cihlar, T., Ho, E. S., Lin, D. C., & Mulato, A. S. (2001). Human renal organic anion transporter 1 (hOAT1) and its role in the nephrotoxicity of antiviral nucleotide analogs. *Nucleosides, Nucleotides and Nucleic Acids*, *20*(4-7), 641-648.

Côté, A. M., Sobela, F., Dzokoto, A., Nzambi, K., Asamoah-Adu, C., Labbé, A. C. ... & Pépin, J. (2004). Transactional sex is the driving force in the dynamics of HIV in Accra, Ghana. *Aids*, *18*(6), 917-925.

Crum-Cianflone, N., Eberly, L., Zhang, Y., Ganesan, A., Weintrob, A., Marconi, V. ... & Wegner, S. (2009). Is HIV becoming more virulent? Initial CD4 cell counts among HIV seroconverters during the course of the HIV epidemic: 1985–2007. *Clinical Infectious Diseases*, *48*(9), 1285-1292.

Currier, J. S., Spino, C., Grimes, J., Wofsy, C. B., Katzenstein, D. A., Hughes, M. D. ... & Cotton, D. J. (2000). Differences between women and men in adverse events and CD4+ responses to nucleoside analogue therapy for HIV infection. The Aids Clinical Trials Group 175 Team. *Journal of acquired immune deficiency syndromes (1999)*, *24*(4), 316-324.

Daugas, E., Rougier, J. P., & Hill, G. (2005). HAART-related nephropathies in HIVinfected patients. *Kidney international*, *67*(2), 393-403.

DeJesus, E., Berger, D., Markowitz, M., Cohen, C., Hawkins, T., Ruane, P. ... & McColl, D. (2006). Antiviral activity, pharmacokinetics, and dose response of the HIV-1 integrase inhibitor GS-9137 (JTK-303) in treatment-naive and treatmentexperienced patients. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *43*(1), 1-5.

DeJesus, E., Herrera, G., Teofilo, E., Gerstoft, J., Buendia, C. B., Brand, J. D., ... & Lanier, E. R. (2004). Abacavir versus Zidovudine combined with lamivudine and Efavirenz, for the treatment of antiretroviral-naive HIV-infected adults. *Clinical Infectious Diseases*, *39*(7), 1038-1046.

Denue, B. A., Gashau, W., Bello, H. S., Kida, I. M., Bakki, B., & Ajayi, B. (2013). Relation between some haematological abnormalities, degree of immunosuppression and viral load in treatment-naïve HIV-infected patients/Relation entre des anomalies hématologiques, le degré d'immunosuppression et la charge virale chez des patients infectés par le VIH et n'ayant jamais reçu de traitement. *Eastern Mediterranean Health Journal*, *19*(4), 362.

Di Mascio, M., Markowitz, M., Louie, M., Hurley, A., Hogan, C., Simon, V. ... & Perelson, A. S. (2004). Dynamics of intermittent viremia during highly active antiretroviral therapy in patients who initiate therapy during chronic versus acute and early human immunodeficiency virus type 1 infection. *Journal of virology*, *78*(19), 10566-10573.

Enawgaw, B., Alem, M., Addis, Z., & Melku, M. (2014). Determination of hematological and immunological parameters among HIV positive patients taking highly active antiretroviral treatment and treatment naïve in the antiretroviral therapy clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study. *BMC hematology*, *14*(1), 1.

Eschedor, J. F., Gordon, J. K., & Duffy, E. (2002). Include UTI in Older Adults' Differential Diagnosis of Syncope. *The Nurse Practitioner*, *27*(3), 66-71.

Erhabor, O., Babatunde, S., & Uko, K. E. (2006). Some haematological parameters in plasmodial parasitized HIV-infected Nigerians. *Niger J Med*, *15*(1), 52-55.

Eron, J. J., Benoit, S. L., Jemsek, J., MacArthur, R. D., Santana, J., Quinn, J. B., ... & Rubin, M. (1995). Treatment with lamivudine, Zidovudine, or both in HIVpositive patients with 200 to 500 CD4+ cells per cubic millimeter. *New England Journal of Medicine*, *333*(25), 1662-1669.

Fisch bach, F.T and Dunning, M.B. (2009). A manual of laboratory and diagnostics tests. Lippincott Williams and Williams.

García-Samaniego, J., Rodríguez, M., Berenguer, J., Rodríguez-Rosado, R., Carbó, J., Asensi, V., & Soriano, V. (2001). Hepatocellular carcinoma in HIV-infected patients with chronic hepatitis C. *The American journal of gastroenterology*, *96*(1), 179-183.

GASCOP. (2002). Clinical Guidelines on antiretroviral Therapy. GASCOP, Accra.

Garred, P. (1998). Chemokine-receptor polymorphisms: clarity or confusion for HIV-1 prognosis? *The Lancet*, *351*(9095), 2-3.

German, R. R., Lee, L. M., Horan, J. M., Milstein, R., Pertowski, C., & Waller, M. (2001). Updated guidelines for evaluating public health surveillance systems. *MMWR Recomm Rep*, *50*(1-35).

Gilks, C, and Victoria M. (2006). Antiretroviral Therapy for HIV infection in Adults and Adolescents in Resource –Limited setting: towards Universal Access: Recommendations for a Public Health Approach. Press Geneva, Switzerland: World Health Organization.

Granich, R. M., Gilks, C. F., Dye, C., De Cock, K. M., & Williams, B. G. (2009). Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for

elimination of HIV transmission: a mathematical model. *The Lancet, 373*(9657), 48-57.

Gutierrez-Valencia, A., Viciana, P., Palacios, R., Ruiz-Valderas, R., Lozano, F., Terrón, A. ... & Lopez-Cortes, L. F. (2009). Stepped-dose versus full-dose Efavirenz for HIV infection and neuropsychiatric adverse events: a randomized trial. *Annals of internal medicine*, *151*(3), 149-156.

Haque, M. R., & Soonthorndhada, A. (2009). Risk perception and condom-use among Thai youths: findings from Kanchanaburi demographic surveillance system site in Thailand. *Journal of Health, Population and Nutrition*, 772-783.

Haug, R. H. (1998). The course of viremia and antibody seroconversion following human immunodeficiency virus exposure: Busch MD, Satten GA. Am J Med 102: 117, 1997. *Journal of Oral and Maxillofacial Surgery*, *56*(1), 113-114.

Hawkins, T. (2010). Understanding and managing the adverse effects of antiretroviral therapy. *Antiviral research*, *85*(1), 201-209.

HIV, C. (2012). AIDS surveillance report, 2004. Vol. 16. Atlanta, GA: US Department of Health and Human Services, CDC; 2005.

Ibeh B.O., Omodamiro O.D., Ibeh U. and Habu J.B. (2013) Biochemical and haematological changes in HIV subjects receiving winniecure antiretroviral drug in Nigeria. *Journal of biomedical science* 20(1), 1.

Interim WHO Clinical Staging of HIV/AIDS and HIV/AIDS Case Definitions for Surveillance: African Region; WHO/HIV/2005.02

Isgro, A., Mezzaroma, I., Aiuti, A., De Vita, L., Franchi, F., Pandolfi, F., ... & Aiuti, F. (2000). Recovery of hematopoietic activity in bone marrow from human immunodeficiency virus type 1- infected patients during highly active antiretroviral therapy. *AIDS research and human retroviruses*, *16*(15), 1471-1479.

Izzedine, H., Launay-Vacher, V., & Deray, G. (2005). Renal tubular transporters and Antiviral drugs: an update. *Aids*, *19*(5), 455-462.

Jao, J., & Wyatt, C. M. (2010). Antiretroviral medications: adverse effects on the kidney. *Advances in chronic kidney disease*, *17*(1), 72-82.

Juma, A., Njagi, E. N., & Ngeranwa, J. J. (2011). Estimation of reference values for liver function tests for adult population in North-Rift Valley, Kenya. *Asian Journal of Medical Sciences*, *3*(6), 243-249.

Khan, K., Khan, A. H., Sulaiman, S. A., Soo, C. T., & Ahsan, R. (2014). Adverse Effect of Highly Active Anti-Retroviral Therapy (HAART) In HIV/AIDS Patients. *Indian Journal of Pharmacy Practice*, *7*(3), 29.

Kalayjian, R. C., Lau, B., Mechekano, R. N., Crane, H. M., Rodriguez, B., Salata, R. A., ... & Eron, J. J. (2012). Risk factors for chronic kidney disease in a large cohort of HIV-1 infected individuals initiating antiretroviral therapy in routine care. *AIDS (London, England)*, *26*(15), 1907.

Kibaru E.G., Nduati R., Wamalwa D. and Kariuki N. (2015) Impact of highly active antiretroviral therapy on hematological indices among HIV-1 infected children at Kenyatta National Hospital-Kenya: retrospective study. *AIDS research and therapy* 12(1), 1.

Kibaya, R. S, Bautista, C. T., Sawe, F. K., Shaffer, D. N., Sateren, W. B., Scott, P. T., Michael, N. L., Robb, M. L., Deborah, L., Birx, D. L and de Souza, M. S., (2008). References Ranges for the clinical laboratory derived from a rural population in Kericho, Kenya, *PLoS ONE*, 3: 10, and 1-7.

Kramer, J. R., Giordano T. P., and El–Serag, H. B. (2007). Effect of Human Immunodeficiency Virus and antiretroviral on outcomes of Hepatitis C: A Systematic Review from an epidemiologic perspective. *Clinical Gastroenterology and Hepatology*, 5: 1321–1328.

Larry, D., Shikuma, C. and Gerschenson, M. (2004). Mitochondrial injury in the pathogenesis of antiretroviral-induced hepatic steatosis and lactic academia. *Mitochondrion*, 4: 95-109.

Levine MA, Berhane K, Karim et al. Prevalence and correlation of anaemia in a large cohort study of HIV infected women: women interagency HIV study. Journal of acquired Immune Deficiency Syndrome. 2004; 269 (1): 28-35.

McMillan, R. (2007, October). The pathogenesis of chronic immune thrombocytopenic purpura. In *Seminars in hematology* (Vol. 44, pp. S3-S11). WB Saunders.

Michaelis, B. A., & Levy, J. A. (1987). Recovery of human immunodeficiency virus from serum. *JAMA*, *257*(10), 1327-1327.

Ministry of Health & Ghana Health Service, 2010, Guide Lines for Antiretroviral Therapy in Ghana (pp.1-95).

Miquez Burbano MJ et al. Limited impact of highly active antiretroviral therapy in Thrombocytopenia. Journal of acquired immune deficiency syndrome. 30(2): 260-261, 2002.

Monforte, A. D. A., Lepri, A. C., Rezza, G., Pezzotti, P., Antinori, A., Phillips, A. N. ... & Caggese, L. (2000). Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naive patients. *Aids*, *14*(5), 499-507.

Moyle, G. (2002). Anaemia in persons with HIV infection: Prognostic marker and contributor to morbidity. *AIDS Reviews*.

Murray, R. P. N. R., Connett, J. E., & Anthonisen, (2002). Smoking and lung function of Lung Health Study participants after 11 years. *American journal of respiratory and critical care medicine*, *166*(5), 675-679.

Mwamburi D.M., Wilson I.B., Jacobson D.L., Spiegelman D., Gorbach S.L., Knox T.A. and Wanke C.A. (2005) Understanding the role of HIV load in determining weight change in the era of highly active antiretroviral therapy. *Clinical infectious diseases* 40(1), 167173.

Ngala R.A., Opoku D. and Asare G. (2015) Effects of HIV infection and highly active antiretroviral therapy (HAART) on the liver of HIV patients. *Trends in Medical Research* 10(1), 1-11.

Ngugi, E. N., F. A. Plummer, J. N. Simonsen, D. W. Cameron, M. Bosire, P. Waiyaki, A. R. Ronald, and J. 0. Ndinya- Achola. 1988. Prevention of transmission of human

immunodeficiency virus in Africa: effectiveness of condom promotion and health education among prostitutes. Lancet ii: 887-890.

Núñez, M. and Soriano, V. (2005). Hepatotoxicity of antiretroviral: incidence, mechanisms and management. *Drug Safety*, 28: 53-66.

Núñez, M. J., Martín-Carbonero, L., Moreno, V., Valencia, E., Garcia-Samaniego, J., Castillo, J. G. D., ... & Soriano, V. (2006). Impact of antiretroviral treatmentrelated toxicities on hospital admissions in HIV-infected patients. *AIDS Research & Human Retroviruses*, *22*(9), 825-829.

O'Brien, M. E., Clark, R. A., Besch, C. L., Myers, L. and Kissinger, P. (2003). Patterns and correlates of discontinuation of the initial HAART regimen in an urban outpatient cohort. *Journal Acquired Immune Deficiency Syndromes*, 34: 407–414.

Obirikorang C., Selleh P., Abledu J. and Fofie C. (2014) Correction: Renal Function in Ghanaian HIV-Infected Patients on Highly Active Antiretroviral Therapy: A CaseControl Study.

Odunukwe, N., Idigbe, O., Kanki, P., Adewole, T., Onwujekwe, D., Audu, R., & Onyewuche, J. (2005). Haematological and biochemical response to treatment of HIV-1 infection with a combination of nevirapine + stavudine + lamivudine in Lagos Nigeria. *Turkish Journal of Haematology*, *22*, 125–131.

Ogundahunsi, O.A. Akinleye, V. A., Oyegunle, A. A., Amballi, and Mbacham, W. (2008). The prevalence of renal disorder in HIV/AIDS patients on HAART. *International Journal of Biomedical and Health Sciences*, 4: 1-4.

Owiredu W., Quaye L., Amidu N. and Addai-Mensah O. (2013) Renal insufficiency in Ghanaian HIV infected patients: need for dose adjustment. *African health sciences* 13(1), 101-11

Pataki, G. E. (2006). Managing side effects of HIV medication. Department of Health, State of New York. Rev.11.

Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med. 1998; 338:853-60.

Palella, F. J., Delaney, K. M., Moorman, A. C., Loveless, M. O., Fuhrer, J., Satten, G.

A., … Holmberg, S. D. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *The New England Journal of Medicine*, *338*(13), 853–60. doi: 10.1056/NEJM199803263381301.

Palella FJ, Baker RK, Moorman AC, Chmiel JS, Wood KC, Brooks JT, and Holmberg SD: Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune Defic Syndr 2006, 43:27–34.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 10, 2011. AIDS info. Available at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf. Accessed January 11, 2011.

Pechere M, Samii K, Hirschel B. HIV-related thrombocytopenia. *N Engl J Med* 1993; 328(24):1785-6.

Pereira, C. F., & Paridaen, J. T. M. L. (2004). Anti-HIV drug development--an overview. *Current Pharmaceutical Design*, *10*(32), 4005–37. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15579085.

Piliero PJ. Pharmacokinetic properties of nucleoside/nucleotide reverse transcriptase inhibitors. J Acquir Immune Defic Syndr. 2004; 37: S2-S12.

Piot, P., Bartos, M., Ghys, P. D., Walker, N., & Schwartländer, B. (2001). The global impact of HIV/AIDS. *Nature*, *410*(6831), 968-973.

Pluda, J. M., Mitsuya, H., & Yarchoan, R. (1991). Hematologic effects of AIDS therapies. *Hematology/oncology Clinics of North America*, *5*(2), 229–48. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/170875916.

Prejean, J., Song, R., Hernandez, A., Ziebell, R., Green, T., Walker, F. ... & Hall, H. I. (2011). Estimated HIV incidence in the United States, 2006–2009. *PloS one*, *6*(8), e17502.

Puhan MA, Van Natta ML, Palella FJ, Addessi A, Meinert C, Ocular Complications of AIDS Research Group. Excess mortality in patients with AIDS in the era of highly active antiretroviral therapy: temporal changes and risk factors. Clin Infect Dis. Oct 15 2010; 51(8):947-56.

Ramana K. and Rao R. (2013) Human immunodeficiency virus disease management in highly active antiretroviral therapy era: a comprehensive review. *Annals of Tropical Medicine and Public Health* 6(1), 5.

Rao, T. S. (2001). Human immunodeficiency virus infection and renal failure. *Infectious disease clinics of North America*, *15*(3), 833-850.

Rimsky, L. T., Azijn, H., Tirry, I., Vingerhoets, J., Mersch, R., Kraus, G. ... & Picchio, G. (2009). In vitro resistance profile of TMC278, a next generation NNRTI: evidence of a higher genetic barrier and a more robust resistance profile than first generation NNRTIs. *Antiviral Therapy*, *14*(4), A141-A141.

Rivero, A., Mira, J. A., & Pineda, J. A. (2007). Liver toxicity induced by non-nucleoside reverse transcriptase inhibitors. *Journal of antimicrobial chemotherapy*, *59*(3), 342-346.

Röling, J., Schmid, H., Fischereder, M., Draenert, R., & Goebel, F. D. (2006). HIVAssociated Renal Diseases and Highly Active Antiretroviral Therapy—Induced Nephropathy. *Clinical Infectious Diseases*, *42*(10), 1488-1495.

Rossen R.D., Butler W.T., Waldman R.H., Alford R.H., Hornick R.B., Togo Y. and Kasel J.A. (1970) The Proteins in Nasal Secretion: II. A Longitudinal Study of IgA and Neutralizing Antibody Levels in Nasal Washings From Men Infected With Influenza Virus. *JAMA* 211(7), 1157-1161.

Sanders, E., J., Graham, S. M. and Okuku, H. S. (2007). HIV-1 infection in high risk men who have sex with men in Mombasa, Kenya. *AIDS*, 21: 2513–2520.

Saville, R. D., Constantine, N. T., Cleghorn, F. R., Jack, N., Bartholomew, C., Edwards, J., & Blattner, W. A. (2001). Fourth-generation enzyme-linked immunosorbent assay for the simultaneous detection of human immunodeficiency virus antigen and antibody. *Journal of clinical microbiology*, *39*(7), 2518-2524.

.Scadden DT, Zon LI, Groopman JE: Pathophysiology and management of HIVassociated haematologic disorders. Blood 1989, 74(5):1455–1463.

Schneider, E., Whitmore, S., Glynn, K. M., Dominguez, K., Mitsch, A., McKenna, M. T., & Centers for Disease Control and Prevention (CDC). (2008). Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged< 18 months and for HIV infection and AIDS among children aged 18 months to< 13 years—United States, 2008. *MMWR Recomm Rep*, *57*(RR-10), 1-12.

Schwarcz S, Richards TA, and Frank H, et al. Identifying barriers to HIV testing: personal and contextual factors associated with late HIV testing. AIDS Care 2011; 23(7):892-900.

Shaunak S, Bartlett JA. Zidovudine induced neutropenia: are we too cautious? Lancet 1989; 334:91-92

Shen L, Peterson S, Sedaghat A, et al. Dose-response curve slope sets class-specific limits on inhibitory potential of anti-HIV drugs. Nat Med. 2008; 14:762-766.

Sloand EM, Maciejewski J, Kumar P, Kim S, Chaudhuri A, Young N. Protease Inhibitors stimulates haematopoiesis and decrease apoptosis and ICE expression in CD34 (+) cells. Blood. 2000; 96:2735.

Smith C, Data Collection on Adverse Events of Anti-HIV drugs (D: A: D) Study Group: TDCoAEoA-HIVdS: factors associated with specific causes of death amongst HIV-positive individuals in the D: A: D study. AIDS 2010, 24:1537–1548.

Soriano V, de Mendoza C. Genetic mechanisms of resistance to NRTI and NNRTI. HIV Clin Trials. 2002; 3237-248.

Spivak JL, Barnes DC, et al, serum immunoreactive erythrocytopenia in HIV infected patients. JAMA 1989; 261:3104-3107. Stiehm E.R. and Fudenberg H.H. (1966) Serum levels of immune globulins in health and disease: a survey. *Pediatrics* 37(5), 715727.

Strategies for Management of Antiretroviral Therapy (SMART) Study Group. (2008). Major clinical outcomes in antiretroviral therapy (ART)–naive participants and in those not receiving ART at baseline in the SMART study. *Journal of Infectious Diseases*, *197*(8), 1133-1144.

Stein N, Korvick J, and Vermunal SH: CD4 + lymphocyte cell enumeration for prediction of clinical course of human immuno deficiency virus disease: a review. J Infect Dis 1992, 165:352–363.

Stellbrink HJ, Orkin C, Arribas JR, Compston J, Gerstoft J, Van Wijngaerden E. Comparison of changes in bone density and turnover with abacavir-lamivudine versus tenofovir-emtricitabine in HIV-infected adults: 48-week results from the ASSERT study. Clin Infect Dis. Oct 15 2010; 51(8):963-72.

Stevenson et al, the pathogenesis of HIV 1. Nature Medicine 9,853-860(2003), doi10.1038/nm0703-853.

Strang AL, Cameron J, Booth C, Garcia A, Geretti AM. Genotypic co-receptor tropism: correlation with enhanced Trofile. Abstract 80. Stockholm, Sweden: 7th European HIV Drug Resistance Workshop. March 25-27, 2009.

Sulkowski, M. S., Thomas, D., Chaisson, R. E. and Moore, R. (2000). Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. *Journal of the American Medical Association,* 283: 74–80.

Sulkowski MS: Drug-induced liver injury associated with antiretroviral therapy that includes HIV-1 protease inhibitors. Clin Infect Dis 2004, 38(S 2): S90–S97.

Sullivan, T. M., Strachan, M., & Timmons, B. K. (2007). *Guide to monitoring and evaluating health information products and services*. USAID.

Thompson, M. (2011). Liver, Kidney, Bone: Emerging Issues of Long Term Antiretroviral Therapy. *20th Annual HIV Conference of the Florida/Caribbean AIDS Education and Training*

Torpey K, Asare R Nyarko C, Agyeman P et al, 2004. Anaemia in patients Accessing Antiretroviral Therapy in Ghana. Int. Conf. AIDS. 16: 15-8. Accessed on 5th August, 2009.

TS LI R, Tubiana, B Autran, 1998. Long-lasting recovery in CD4 T-cell function and viral-load reduction after highly active antiretroviral therapy in advance HIV-1 disease. Science Direct, doi: 10.10, vol.351 (9117): 1682-1686.

UNAIDS. (2011). UNAIDS World AIDS Day Report, Geneva, Switzerland.

UNAIDS/World Health Organization. United Nations 2007 AIDS Epidemic Update. UNAIDS. Accessed October 6, 2008.

UNICEF (2009). Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress Report 2009. In *Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report 2009*. OMS

U.S. Food and Drug Administration Antiviral Drugs Advisory Committee Meeting. May 13, 2003.

Venkataramana K. (2013) A study of biological markers in HIV disease progression and management in the highly active antiretroviral therapy (HAART) era. *American Journal of Bioscience and bioengineering* 1(2), 24-37.

Volberding P.A, Lagakos SW, Koch MA et al. Zidovudine in asymptomatic HIV infections. N Engl J Med 1990; 322: 941-949.

Volberding P.A., Levine A.M., Dieterich D., Mildvan D., Mitsuyasu R., Saag M. Anemia in HIV infection.

Waithaka, S. K., Njagi, E. N., Ngeranwa, J. N. and Kigondu C. S. (2009). Reference Ranges for Some Biochemical Analytes in Adult Kenyans. *International Journal of Health Research,* **2**: 259-266.

Walmsley S, Antela A, Clumeck N, et al. Dolutegravir (DTG; S/GSK1349572) + Abacavir/Lamivudine Once Daily Statistically Superior to Tenofovir/Emtricitabine/Efavirenz: 48-Week Results - SINGLE (ING114467). Abstract presented at: 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). Sept 2012; Abstract H-556b:

Watkins BA, Dom HH, Kelly WB: Specific tropism of HIV-1 for microghaceus in primary human brain culture. Sci 1990, 249(4968):549–553.

Waller RE, Paller RI, Kovacs JA, et al. Anaemia and erythropoiesis in patients with AIDS and Kaposi's sarcoma treated with Zidovudine. Ann. Intern. Med. 1988; 108: 372-376.

Warnke D, Barreto J, Temesgen Z. Antiretroviral drugs. J Clin Pharmacol. 2007; 47:1570-1579.

WHO. (2009) b. Guidelines for HIV Diagnosis and Monitoring of Antiretroviral Therapy, WHO Project: ICP BCT 001, SEA-HLM-382 (Rev. 1).

When to start ART in Adults and Adolescents Consolidated ARV guidelines, June 2013; WHO Guide Report: 6; 2013.

Wit, F. N., Weverling, G. J., Weel, J., Juriceans, S., and Lange, J. M. (2002). Incidence of and risk factors for severe hepatotoxicity associated with antiretroviral combination therapy. *Journal of Infectious Diseases,* 186: 23–31.

Winkelstein, W., Jr., D. M. Lyman, N. Padian, R. Grant, M. Samuel, J. A. Wiley, R. E. Anderson, W. Lang, J. Riggs, and J. A. Levy. 2006. Sexual practices and risk of infection by the human immunodeficiency virus: The San Francisco Men's Health Study. JAMA 257:321-325.

Wofsy, C. B., J. B. Cohen, L. B. Hauer, N. S. Padian, B. A. Michaelis, L. A. Evans, and J. A. Wohl DA, Brown TT. Management of morphologic changes associated with antiretroviral use in HIV-infected patients. J Acquir Immune Defic. 2008 49: S93-S100.

Wyatt, C. M., Morgello, S., and Katz-Malamed, R. (2009). The spectrum of kidney disease in patients with AIDS in the era of antiretroviral therapy. *Kidney International*. 75: 4:428–434.

Zhang, L. Q., P. Simmonds, C. A. Ludlam, and A. J. L. Brown. 1991. Detection, quantification and sequencing of HIV-1 from the plasma of seropositive individuals and from factor VIII concentrates. AIDS 5:675-681.

APPENDIX 1

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
1	1	5.11	1.78	2.11	2.92	7.9	457	37.7	9.2	17.5	54.8	113.5	3.59	80562
2	1	2.9	1.11	1.06	4.66	12.9	229	39.6	6	17.5	77.4	110.6	2.5	23610
3	1	1.95	0.39	0.98	6.66	22.8	73	40.1	22.5	42.7	115.6	114.6	2.96	2264288
4	1	5.3	2.26	2.32	3.82	11.3	189	34.7	53.4	77.7	77.2	133.6	5.18	386978
5	1	1.15	0.56	0.47	8.69	26.1	48	41.5	47	70.3	28	114.9	3.33	624596
6	1	0.89	0.44	0.37	8.3	24.5	32	40.1	26.6	29.9	65.7	102.1	3.06	174931
7	1	5.36	2.42	2.33	4.32	10.9	350	37.9	6.7	16.6	92.7	103.2	3.27	145619
8	1	3.19	1.36	1.12	3.48	9.4	194	18.5	9.4	34	68.3	50.9	2.13	103531
9	1	5.36	3.08	1.33	3.81	9.6	261	37.6	10.4	19.3	51.5	90.7	1.56	23887
10	1	3.56	1.63	1.11	3.38	10	150	40.2	65.6	89.1	68.8	101.8	4.31	124393
11	1	2.63	1.09	0.91	3.43	12.6	221	44.1	42.9	111	65.8	115.9	6.52	108932
12	1	18.87	14.7	2.78	3.9	11.3	619	5.9	34.6	74.4	50	51	6.06	87396
13	1	1.44	0.64	0.65	9.3	27.8	33	46.9	17.1	17.4	50	118.7	4.98	18914
14	1	6.43	4.17	3.87	9.2	25.6	36	41.8	8.2	18.7	53	99.9	2.53	272791
15	1	5.58	2.3	2.97	2.97	8.9	147	41.4	15.3	40.6	53.8	114.9	3.62	224146
16	1	4.75	1.4	2.33	3.84	10.8	201	45.2	33.4	33.2	71.6	85.9	3.01	851903
17	1	0.73	0.37	0.26	3.22	10.5	119	3.7	119.9	94.1	71.1	47.3	3.82	375195
18	1	3.97	1.41	2.1	2.28	8.7	251	37.6	20.5	45.4	79	114.8	3.27	150491
19	1	3.52	1.1	1.5	5.2	14	104	8.4	18.8	29.5	80.1	64.2	2.99	73108
20	1	5.56	2.91	1.82	2.99	9.9	313	13.7	>250.0	215.7	56.3	72.1	1.23	1083615
21	1	4.98	1.35	2.66	3.71	10	258	10.3	0	14.4	65.7	46.9	2.27	36
22	1	5.23	3.78	0.88	3.25	12.4	276	35.7	18.9	68.5	113.1	99.1	8.89	380943
23	1	4.56	1.47	2.03	2.79	10	229	44.1	13.5	17.5	51.5	100.2	2.24	486

24	1	3.72	1.92	1.34	2.4	7.9	78	5.4	22.1	34.4	121.9	25.8	5.14	166910
25	1	9.24	5.41	2.7	3.32	9.7	353	37.7	45.8	19.7	69.7	82.6	5.19	15642
26	1	4.24	1.82	1.38	3.72	12.6	172	42	19	18	76	92	2.2	86535
27	1	8.11	4.15	3.09	2.93	9	413	38.4	61	43.2	166.7	106	9.63	146320
28	2	3.64	1.87	1.05	3.05	9.8	242	38	58	42	98	75	2.9	Target not Detected
29	1	6.73	2.97	2.78	4.67	14.6	283	45.7	14.9	29.4	113.4	110.7	3.35	115774
30	1	3.25	1.95	1.06	0.77	9.3	112	31.3	19.3	47.7	55.3	101.3	3.87	154485
31	1	4.12	1.59	1.49	3.69	11.8	188	47.4	21.9	38.7	86.3	108.5	2.62	18794
32	1	6.37	4.02	1.52	3.97	13.1	141	40.9	6.7	27.3	34.5	85.9	2.71	7063
33	2	4.86	3.28	1.03	3.25	8.6	94	43.2	46.7	18.2	75.2	28.2	3.07	Target not Detected
34	1	4.14	1.81	1.73	3.9	10.7	182	37.9	13.8	19.9	78	115.5	4.96	69913
35	1	7	5.33	0.88	2.48	8.9	289	36	19.8	38.4	63.3	97.3	0.97	418310

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
36	1	7.74	6.52	0.93	3.42	8.5	128	33.8	18.2	17.2	125.3	72.7	12.6	73186
37	1	2.52	1.54	0.69	2.68	6.9	139	38.2	14.5	24.1	116	83	6.5	2276274
38	1	2.24	1.11	0.77	4.04	11.9	163	44.2	22.9	30.7	58.7	90.2	2.57	283914
39	1	4.4	6.42	2.4	3.98	12.1	205	42	14	18	87	76	5	60527
40	1	7.41	5.99	0.62	2.48	6.9	434	25	41	50	99	70	4.2	1162621
41	1	7.11	4.58	1.71	2.91	10.3	158	37	8.7	12.9	46.4	71.3	2.62	367011
42	2	4.75	2.22	1.64	3.22	9.7	161	40.6	7.6	11	39.8	80.3	1.31	Target not Detected
43	1	4.58	2.26	2.02	4.17	11.1	346	36	13.9	27.8	114.9	82.5	3.6	51231
44	1	4.9	2.24	1.52	3.2	7.8	227	37	6	10	44.7	87	8.6	77265
45	1	5	4.2	2.03	3.97	9.7	324	32	5	5	55.8	80	2.6	44267
46	1	5.64	2.66	2.3	3.8	9.8	316	32.3	13.4	22.1	67.1	78.7	2.6	23169
47	1	1.98	0.97	0.51	3.67	10.9	203	45.1	35.4	20.8	109.1	80.8	5.9	NIL
48	1	4.53	2.66	1.17	3.27	10.3	355	39.9	29.5	35	63.4	100.3	4.53	NIL
49	1	4.3	2.24	1.19	3.21	9.8	279	26.7	87.8	141.1	71	67	3.53	8963
50	1	3.47	1.25	1.68	3.86	11.2	229	41.9	17.4	36	102.3	80.6	2.7	NIL

51	1	5.4	2.34	2.13	5.56	15.3	134	44.5	22.3	20.8	98.8	100.4	2.24	NIL
52	2	2.1	0.64	1.12	4.26	9.4	207	35.6	39.7	93.6	78.5	85.2	2.6	Target not Detected
53	1	8.52	7.47	0.48	3.9	8.5	322	35.5	69.8	64.3	181.7	81.6	7.6	116827
54	1	3.1	1.46	1.25	3.75	10.4	268	43	10	13	90	101	4.1	96245
55	1	2.61	1.07	0.94	2.76	8.2	201	31.4	4.2	6.3	83.5	104.1	1.28	345693
56	1	9.01	7.89	0.68	3.91	9.7	587	34	31	32	121	76	7.4	1904381
57	1	4.23	1.86	1.8	4.52	12.9	244	48	12	14	85	82	3.7	679204
58	1	6.37	2.73	3.03	3.57	9.2	213	22	45	46	78	67	3.1	NIL
59	1	6.52	2.1	3.2	3.26	8.3	201	54.2	30.3	40.2	88.7	94.9	4.3	710819
60	1	3.95	1.81	1.63	3.47	11.5	138	55.6	19.2	22.7	43.9	103.7	2.7	6365
61	1	1.94	2.5	2.16	2.49	8.79	126	18.8	62	88.6	97	77.1	5.63	461515
62	2	2.5	1.75	2.11	3.65	9.8	126	41	28	29	70	92	2.1	Target not Detected
63	1	5.78	3.71	1.48	2.79	6.8	305	39.3	38	37.2	77.9	75.7	2.55	63927
64	1	6.4	3.42	1.87	4.56	12.1	290	40	23	81	71	81	3.2	97624
65	1	5.7	2.67	1.33	3.8	6.7	282	37.1	13.2	25.3	106.7	84.6	4.71	89473
66	1	5.45	2.98	2.11	4.66	12.8	337	40	55	50	83	85	2.6	269527
67	1	7.75	4.82	2.12	3.22	11.1	155	37.8	7.4	30.2	104.2	101.2	2.46	NIL
68	1	9.23	2.24	6.42	2.83	10.3	234	65.7	19.3	24.6	143.4	83.2	4.67	28283
69	1	7.23	3.41	3.06	3.34	8.4	198	34.4	51.3	35.1	50.2	61.9	4.56	16097
70	1	5.05	1.63	1.05	3.12	10.3	142	41.9	14.6	26.7	92.2	89.3	2.67	1010487

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
71	1	4.98	8.5	2.06	2.87	9.5	195	53.8	11	26.5	135.9	91.4	7.89	78416
72	1	3.6	2.19	1.8	4.02	9.2	236	40	19	22	74.7	92	9.27	19358
73	1	2.56	1.03	0.93	7.23	25.9	25	47.6	11.7	48.5	131.3	106.4	5.33	91873
74	1	2.92	0.7	3.51	5.14	10.33	190	41.37	52.3	31.4	158.1	85.9	3.78	17426
75	1	7.63	2.57	2.55	4.01	8.7	250	41.2	25.1	34.9	135	101.2	3.99	57479
76	1	7.02	1.97	2.49	3.39	12.1	310	49.9	11.5	21.7	85	80.5	3.2	705954
77	2	6.99	2.91	3.1	4.13	10.8	275	50.1	13.2	29.7	125.7	52.8	5.14	67318
78	1	7.32	1.47	3.91	4.15	10.7	290	48.1	8.9	22.8	130.3	99.9	3.36	440869
79	1	6.6	2.23	3.55	3.43	11.2	200	44.8	11.7	20.3	131	105.3	5.7	182634
80	1	5.65	1.6	2.3	4.29	10.4	260	39.6	16.4	250	167.3	94.5	1.9	981526

81	1	7.93	1.4	5.42	3.32	10.9	285	28.8	101.8	106.9	52.1	91.5	5.57	12676
82	1	2.34	1.46	0.46	1.67	5.5	197	40.5	30.6	49.7	93.4	113.7	5.36	603589
83	1	5.6	2.25	4.67	6.47	22.1	64	51.1	26.4	27.9	84.2	101.1	2.43	224146
84	1	2.5	0.76	0.82	7.29	25.9	49	45.9	44.3	45.1	84.7	76.2	3.67	131786
85	1	4.9	0.78	2.96	2.95	11.2	280	43.9	24.3	22.8	65.9	88.3	1.82	44071
86	1	4.4	1.51	2.4	3.48	11.5	214	42.6	26	27.9	69	61.9	2.12	33870
87	1	5.19	1.3	4.19	2.01	9.2	234	47.5	15.1	23.1	85.4	81.9	2.87	38589
88	1	3.96	1.88	1.39	7.43	23.1	61	42.4	17	18.7	58.8	91.1	3.34	609437
89	1	3.97	1.64	1.66	3.3	9.4	310	41.6	20.8	23.3	80.9	97.4	2.15	872614
90	1	4.38	2.09	1.86	4.14	10.9	215	44.6	42.3	34.7	87.9	78.8	2.12	84675
91	1	5.82	2.59	2.19	3.86	10.4	310	45.9	17.9	28.2	57.5	79.2	2.16	534617
92	1	3.73	0.96	2.27	2.78	8.8	101	43.7	28.9	20.1	74.5	83.6	5.15	72603
93	1	4.27	1.61	2.36	3.4	10.9	240	44.9	21.7	36.5	63.5	85.2	4.9	203614
94	1	7.96	1.76	4.89	4.63	13.4	170	43.2	44.5	41.7	121.7	100.3	3.71	291683
95	1	5.98	2.87	2.55	3.33	12.1	142	43.9	18.7	13.9	78.8	101.1	3.21	796158
96	1	4.04	1.89	1.37	6.79	19.3	90.6	45.1	17.1	25.3	81.9	90.7	3.11	30867
97	1	4.85	1.23	5.38	3.33	12.7	249	50.3	53.3	30.7	71.6	94.9	6.1	425839
98	1	4.79	1.57	3.46	3.68	10.34	200	48.6	55.9	38.1	50	83.1	2.58	93173
99	2	8.33	3.2	3.9	4.36	14.2	62	48.5	27.6	33.8	98	102.4	5.62	Target not Detected
100	1	5.13	4.21	3.43	3.26	12.7	187	43.2	27.5	41.1	102.2	110.5	4.18	324892
101	1	7.24	4.91	4.18	3.13	11.8	237	50.4	38.9	25.9	86.5	99.3	2.64	20316
102	1	6.12	5.6	3.91	2.94	9.37	224	47.9	49.7	51.2	54.9	81.1	1.16	375914
103	1	5.89	3.1	6.48	4.18	10.3	280	42.7	19.4	32.7	36.8	100.7	3.11	215728
104	1	7.89	2.71	2.97	6.8	10.7	157	0.9	23.1	22.2	0.2	100.7	3.23	2187
105	1	8.61	0.83	3.13	5.8	11.3	427	43.1	20.5	25.3	56.8	87.3	3.16	54325

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
106	1	13.48	4.42	7.13	6.32	12.4	500	45.1	33.2	37.4	43.4	92.1	3.83	8963
107	1	9.4	5.23	7.27	5.44	10.9	370	46.3	44.5	22.4	34.7	79	3.47	66134
108	1	8.61	4.47	2.9	6.8	12.4	429	53.1	34.3	35.3	37.5	97.8	2.05	92709
109	1	5.34	3.5	5.91	6.1	11.9	210	59.7	30.9	30.8	45.1	100.5	3.21	10975

110	1	10.78	2.98	4.76	6	12.3	330	47.9	21	22.5	49.2	100.8	2.02	95258
111	1	5.3	5.13	1.67	3.3	12.6	250	51.3	20.8	24.1	31.9	96.2	2.32	12460
112	1	4.24	4.7	3.8	3.24	10.1	320	46.4	28.5	27.8	19.2	99.2	3.22	100413
113	1	6.29	1.96	8.15	5.01	11.2	70	44.7	23.7	30.6	56.6	110.6	3.51	19628
114	1	2.4	4.13	4.82	4.1	11.7	179	41.1	15.5	16.1	30.1	101.6	1.68	158161
115	1	5.37	0.97	6.13	3.1	10.3	270	38.6	54.8	40.3	100.1	70.7	2.67	201763
116	1	5.46	4.27	2.56	5.21	11.3	95	41.1	11.1	18.5	112.4	110.4	5.54	1058
117	1	5.69	2.17	5.22	3.61	12.2	210	50.3	18.9	21.3	35.7	90.4	3.89	23691
118	2	6.99	3.15	2.9	2.37	9.5	265	41.7	22.3	20.2	33.5	83.5	4.96	Target not Detected
119	1	4.65	4.03	2.61	3.1	11.5	261	48.3	16.1	20.2	45.4	90.7	3.11	46353
120	1	4.93	1.9	7.15	3.48	13.3	70	43.6	35.7	21.9	49.7	103.1	4.82	3018547
121	1	5.9	1.06	6.17	3.36	12.9	332	41.9	26.3	19.6	125.7	80	2.89	21605
122	1	3.1	5.02	6.81	4.06	13.1	110	37.4	18.5	20.3	99.2	79.8	1.62	296105
123	1	6.79	3.01	5.31	2.99	12.3	250	50.4	23.9	30.2	126.2	120.1	4.29	1217964
124	1	4.87	3.49	4.13	4.91	13.1	50	49.3	41.9	41.7	123.5	100.5	2.76	71494
125	1	4.78	3.14	2.01	5.48	17.7	129	32	14.8	12.7	66	75.5	3.12	156269
126	1	4.4	3.9	6.89	3.19	9.7	322	34	26.2	34.7	53.7	85.7	1.74	189541
127	1	7.48	5.12	1.53	3.79	10.6	169	29.2	26.2	45.1	91.2	72.7	2.64	53694
128	1	8.9	1.17	7.95	2.66	9.7	130	34.9	26.3	29.5	64.3	80.9	2.59	5096
129	1	3.56	4.83	5.15	3.03	11.5	81	39.1	12.1	18.5	109.2	80.2	1.88	12362
130	1	5.48	5.69	4.8	2.14	10.3	142	41.7	15.3	23.5	94.2	70.9	3.67	20539
131	1	7.24	2.2	5.27	4.75	9.2	371	49.8	31.7	27	99.6	92.9	4.35	67108
132	1	6.87	1.52	5.16	3.11	12.1	210	50.4	35.4	22.6	130.6	91.9	4.57	81645
133	1	5.42	2.13	3.9	4.27	13.3	60	39.1	21.7	23.8	70.7	86.8	2.67	267483
134	1	3.78	3.81	1.38	4.58	16.9	125	38.1	43.6	41.4	70.5	83.9	2.8	100632
135	1	7.83	2.7	5.04	2.94	10.4	240	40.1	17.4	19.3	80.7	74.8	3.49	103645
136	1	7.89	2.1	4.91	2.99	12.2	249	30.2	10.9	14.1	45.1	68.9	2.67	11751
137	1	6.41	1.9	7.13	4.21	12.7	241	35.4	23.5	18.7	90.1	70.1	5.35	193748
138	1	5.94	3.8	6.45	3.41	11.9	213	38.5	22.8	20.3	48.1	76.7	3.09	1096
139	1	4.56	2.5	7.29	6.74	16.88	65	41.9	28.6	23.8	84.3	97.91	3.25	1583279
140	1	5.13	3.9	6.12	3.42	11.8	250	38.1	19.1	19.7	80.1	70.5	2.6	36281

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
141	1	4.93	5.8	3.75	6.01	24	30	33.1	14.6	15.9	52.7	64.7	1.62	602816
142	1	5.38	4.1	6.18	2.82	12	120	42.5	12.7	21.6	43.9	92.3	3.01	59426
143	1	4.7	4.9	6.11	4.06	15.1	110	39.6	17.1	19.7	65.9	83.1	2.17	100285
144	1	9.13	5.2	5.31	4.11	11.3	135	34.4	12.2	14.9	65.3	58.1	2.57	44852
145	1	6.42	1.4	9.02	3.79	12.2	170	35.9	24.2	20.4	85.7	65.1	2.51	33562
146	1	3.21	1.86	1.35	5.11	11.7	270	44.1	9.5	25.8	73.2	59.1	2.7	1896019
147	1	4.97	0.91	1.93	3.19	12.1	70	48.3	37.6	24.3	68.5	60	2.71	69784
148	2	4.75	3.09	2	3.18	14.5	231	41.4	23.9	57.1	74.8	79.4	6.81	Target not Detected
149	1	3.79	1.13	4.07	3.19	10.2	180	51.2	29.8	35.9	121.5	121.1	5.15	214656
150	1	5.98	2.37	3.41	3.13	10.9	161	42.9	53.1	38.8	100.1	98.5	1.9	182064
151	1	5.14	0.97	3.25	3.12	10.5	400	43.1	10.1	24.9	68.1	78.6	3.7	2637148
152	1	6.98	3.83	1.79	3.1	9.5	310	50.6	52.7	43.5	90.6	81.9	2.8	61783
153	1	5.19	1.57	2.91	3.06	12.3	150	53.4	56.2	47.8	126.1	102.3	3.4	89763
154	1	2.13	1.27	3.21	3.2	12.1	190	57.1	30.3	32.9	95.5	81.6	1.9	99716
155	1	3.01	0.9	1.12	3.11	12	240	32.8	42.2	46.1	121.9	95.4	2.8	589263
156	1	3.11	1.16	3.05	3.21	11.5	291	49.1	20.6	28.8	42.9	100.7	1.5	98618
157	1	6.89	1.98	3.59	3.97	11.2	289	53.5	43.1	45.7	100.2	80.3	1.3	15375
158	1	2.76	0.84	0.81	5.84	16.3	61	59.2	51.9	48.3	76.5	90.7	5.1	495728
159	1	3.25	2.06	2.65	3.12	11.1	195	45.3	47.5	52.1	77.2	110.3	2.3	116389
160	1	4.98	1.19	4.24	3.87	11.5	111	40.3	40	31.2	89.8	95.7	2.1	19428
161	1	4.01	2.21	1.44	3.16	12.4	175	50.5	47.1	51.2	63.7	57.9	4.7	50795
162	1	4.95	1.79	4.33	3.47	11.9	301.2	47.8	26.3	28.7	49.2	102.3	4.3	79318
163	1	8.77	1.97	3.76	4.21	12	260	54.9	50.2	23.9	79.6	81.7	2.1	61353
164	1	4.15	1.68	5.22	4.1	12.3	211	43.1	28.3	38.4	81.5	79.8	3.3	693264
165	1	4.91	3.18	2.55	3.81	10.1	130	49.1	34.5	51.9	71.2	98.5	1.5	38261
166	1	6.18	1.9	4.91	3.11	12.2	180	44.5	43.2	22.57	125.1	110.2	2.18	112783
167	1	3.02	1.82	1.95	7.34	19.2	40	51.3	21.9	42.7	74.3	80.4	3.1	492759
168	1	3.47	1.26	1.61	4.11	11.1	139	53.7	42.7	53.2	35.1	99.5	4.25	94621
169	1	4.61	6.51	2.62	9.39	21.3	26	55.2	38.5	15.5	87.8	100.3	4.09	84179
170	1	6.76	3.55	3.41	3.57	10.9	241	54.6	28.4	30.87	35.4	110.2	4.95	197352
171	1	1.58	0.66	4.89	7.12	23.1	23	45.2	30.2	19.9	87.5	80.8	5.2	29745

172	1	3.12	1.72	1.61	4.22	12.1	241	50.8	15.7	50.27	85.8	90.5	2.91	137481
173	1	4.11	1.66	2.32	3.8	13	210	49.1	34.5	16.57	40.7	82.4	5.51	7928
174	1	4.55	1.27	2.83	3.39	12.5	124	41.9	50.5	31.6	31.8	91.7	2.71	13429
175	1	4.97	1.94	2.43	3.21	11.8	175	52.3	31.3	25.54	20.3	101.1	4.89	23165

Id	HIV Type 1or2 or Both	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral loads Results Before Medication(Copies/mL)
176	1	4.72	3.06	1.2	5.63	14.8	85	47.2	15.2	30.47	21.9	104.4	3.69	117528
177	1	7.44	1.97	4.55	4.03	9.8	189	41.3	30.7	45.9	89.1	78.1	2.9	1869217
178	1	5.42	2.62	1.89	4.93	11.1	260	50.8	25.6	10.7	72.9	81.8	3.1	219735
179	1	6.1	1.6	2.8	2.12	11.4	171	12.8	75.2	41.71	49.6	110.4	2.14	37428
180	1	9.67	3.79	4.54	4.25	11.3	320	34.1	19.5	14.7	40.3	83	2.7	11827
181	1	5.34	3.1	1.3	2.13	8.9	553	43.1	46.3	35.5	50.1	99.7	1.59	29256
182	1	10.68	4.26	3.87	3.57	10.1	79	31.5	15.1	9.86	70.1	106.7	2.79	15642
183	1	4.74	1.51	2.13	4.23	10.7	221	54.9	15.9	45.43	72.5	130.1	3.87	146817
184	1	7.04	2.73	3.62	3.91	12.5	301	55.7	25.7	15.09	75	120.5	4.77	120519
o185	1	7.24	4.07	2.15	3.19	10.1	150	31.5	20.8	23.4	67.2	106.5	4.19	416893
186	1	7.94	3.96	2.79	3.11	12.5	310	49	14.6	22.3	73.8	81.1	5.1	17623
187	1	7.08	1.83	4.3	4.78	10.7	146	36.7	26.3	27.04	38.5	100.1	2.13	19694
188	1	9.28	4.4	2.91	3.95	12.1	310	53.6	21.5	35.41	56.5	101.2	3.1	29763
189	1	5.62	1.91	2.57	3.93	10.1	253	47.6	18.5	22.9	80.8	67.2	4.5	26347
190	1	7.6	2.15	4.71	4.51	12.9	70	33.9	42.4	74.7	51.2	101.8	2.9	69622
191	1		1.47	2.21	3.81	9.7	201	56.1	21	25.06	70.3	102.1	3.54	61739
192	1	3.72	0.92	1.87	3.51	9.9	97	45.4	31.7	42.5	73.6	81.9	2.5	63820
193	1	4.27	1.96	1.74	3.4	10.3	290	49.7	55	60.3	64.8	100.5	2.13	38276
194	1	3.28	1.21	1.74	3.91	9.8	45	45.3	30.1	21.1	61.6	83	2.9	34579
195	1	6.59	1.97	3.55	4.01	10.8	343	44.5	42.3	35.6	56.9	80.8	2.7	1208633
196	1	4.22	2.83	0.66	4.31	10.6	357	36.8	22.6	69.8	52.7	116.5	2.49	1034751
197	1	3.31	1.39	1.08	4	10.6	185	55.3	13.5	16.76	23	112.1	2.54	473629
198	1	4.13	1.25	2.05	2.97	9.4	155	32.4	38.9	228.08	107.6	94.4	4.97	32829
199	1	5.49	2.84	1.84	3.38	9.9	319	36.5	24.1	30.5	45.7	100.5	3.2	587474
200	1	5.97	1.92	3.05	4.83	13.7	296	22	82.4	76.4	79.6	41.2	1.5	19509

KEYS: WBC-White Blood cells, RBC- Red Blood cells, HB- Haemoglobin, PLT- Platelet count, ALB- Albumin, ALT- Alanine transaminase, AST- Aspartate aminotransferance, CRbi- Creatinine, PRTB- Total Protein, URSL- Urea, OH- Others, NEUT#-Absolute Neutrophils, LYMP#- Absolute Lymphocytes.

ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads (Copies/mL)
1	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	7.25	2.88	3.12	6.72	9.43	315	40.1	20.5	27.1	78.5	116.3	2.49	49
2	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	5.18	2.46	2	4.51	7.5	274	50.2	31.3	20.5	101.4	95.3	4.68	268
3	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	7.96	2.56	4.61	4.54	9.3	175	45.7	55.5	69.7	73.5	100.3	9.7	356184
4	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	5.98	2.46	1.39	4.23	10.8	215	30.6	38.3	35.1	91.7	86.5	5.12	1447
5	Efavirenz	Lamivudine	Tenofovir	Septrin	Vitafol	4.78	2.17	1.63	3.92	11.3	245	46.4	49	46.83	118.3	128	3.09	1082
6	Efavirenz	Lamivudine	Tenofovir	Septrin	Vitafol	4.29	3.05	1.09	3.79	11.5	186	49.5	51.1	63.5	87.1	108.9	6.08	21579
7	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	5.41	1.96	2.89	5.26	10.1	310	42.7	30.5	24.6	81.4	98.5	4.26	504
8	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	5.21	1.82	1.77	4.71	11.6	230	61.3	20.9	36.1	57.1	65.8	2.11	159
9	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.92	4.13	2.11	5.13	12.1	310	30.5	25.7	30.4	54.5	96.6	2.57	98
10	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	3.24	1.46	1.09	5.74	12.8	205	50.3	47.8	39.5	65.9	105.6	5.31	101
11	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	4.95	2.08	2.31	4.41	13.2	322	41.8	45.8	110.1	69.9	110.7	5.52	396
12	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	8.11	4.5	2.39	4.33	12.4	420	30.8	31.4	81.2	72.6	57.9	5.03	78
13	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.02	4.03	0.85	5.2	11.7	185	40.9	16.1	17.2	55.2	110.1	3.95	<20
14	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.2	2.16	2.03	4.43	10.8	150	59.1	15.6	21.2	54.5	100.3	3.51	2945
15	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	6.32	3.31	2.71	3.81	11.3	160	35.2	20.9	46.3	62.5	110.8	4.51	149942
16	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	6.92	2.51	4.01	4.17	12.1	248	49.1	41.3	53.1	51.4	98.7	6.12	35949
17	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.92	1.62	3.73	5.05	12.9	271	35.6	40	37.1	53.5	102.3	6.4	5158
18	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	6.15	1.92	2.96	4.97	11.5	193	38.8	42.5	31.7	121.7	124.9	5.1	1026
19	Lamivudine	Zidovudine	Nevirapine	Septrin	Zingovite	6.63	4	1.63	4.57	13.4	95	30.3	67.4	58.6	117	101.7	5.9	595
20	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	8	2.86	4.18	3.95	11.8	127	28.9	35.4	62.7	81	91.9	7.3	275035
21	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	3.73	2.56	1.03	5.14	9.9	150	58.1	43.5	48.7	62.4	115.1	3.12	Target not Detected
22	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	3.5	2.67	0.56	3.89	10.6	24.5	38.3	16.8	52.5	109.2	98.9	8.02	513
23	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	10.47	4.15	2.98	4.89	10.8	245	40.5	25.2	31.7	71.5	103.5	3.34	<20
24	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	4.48	1.93	1.03	3.95	10.2	200	10.9	18.5	31.4	119.7	65.8	4.14	2832
25	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	8.13	4.41	2.5	3.12	11.8	280	42.8	47.8	52.9	63.6	85	5.21	Target not Detected
26	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	7.55	2.77	3.59	3.95	13.1	150	40.7	256.2	26.9	80.1	94.8	1.6	187
27	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	8.33	4.03	3.57	4.41	10.2	315	50.2	39.4	34.5	120.1	100.5	7.53	120
28	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	4.35	2.97	1	5.26	11.8	210	50.3	55.2	41.6	78.4	80.1	3.8	Target not Detected
29	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.22	2.69	2.58	4.55	14.1	260	51.9	36.5	41.3	110.2	120.6	3.15	<20

30	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.81	2.65	2.76	4.27	10.6	275	36.5	24.8	41.7	73.2	98.5	2.63	1035
31	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	4.1	1.35	2.01	3.38	11.2	146	58.2	30.5	34.4	81.3	100.5	2.11	135
32	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.76	3.87	1.41	4.15	12.8	140	43.7	10.1	25.5	54.3	91.8	2.8	<20
33	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	3.44	2.17	1	4.39	10.5	138	34.8	35.6	26.1	72.4	101.6	4.8	Target not Detected
34	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	3.52	1.63	1.57	3.84	12	170	40.9	18.6	25.1	110.5	105.1	9.2	396
35	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	4.2	3.2	0.51	3.9	10.4	260	31.5	21.7	40.4	85.1	95.3	4.7	854

ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads (Copies/mL)
36	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.6	3.68	1.71	4.01	10.2	150	37.2	79.3	42.1	125.3	81.3	15.8	375
37	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	2.29	1.24	0.49	4.16	9.2	150	41.4	21.6	30.3	120.3	80.9	9.1	975063
38	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.84	2.15	2.55	4.98	12.5	160	35.9	20.3	35.8	67.8	95.4	4.2	24067
39	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.45	2.53	2.11	4.05	11.9	250	57.3	49.1	54.2	134.9	90.5	8.7	1049
40	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.34	2.89	1.96	3.9	9.5	353	20.4	18.2	43.5	105.1	81.5	3.1	20185
41	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.09	2.98	1.52	2.71	10.1	135	30.9	12.7	20.5	57.4	75.7	2.15	275063
42	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	4.35	2.16	1.44	3.87	10.3	150	42.1	10.6	13.5	48.9	81.7	1.98	Target not Detected
43	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.22	2.85	1.97	4.31	12.7	255	24.9	10.8	25.3	105.2	79.9	2.7	98
44	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	4.88	2.35	2.09	2.41	9.3	185	40.4	9.5	29.1	143.2	95.5	18.9	508
45	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	5.45	1.99	2.03	3.69	9.5	285	41.3	18.4	31.5	71.6	93.5	4.8	159
46	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	4.72	2.13	2.15	3.91	11.3	387	35.6	37.4	35.7	76.4	86.2	2.9	215
47	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	4.57	3.8	0.42	3.87	11.4	135	57.3	32.6	44.7	125.8	101.6	9.2	NIL
48	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.32	2.85	1.93	4.53	13.9	300	50.2	38.4	43.7	83.5	109.3	3.81	NIL
49	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	6.31	2.96	2.37	4.13	12.2	130	30.8	79.3	110.6	53.1	74	4.2	Target not Detected
50	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.12	3.08	2.16	4.11	13.6	155	46.2	30.7	25.1	134.1	103.4	10.8	NIL
51	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.96	3.19	2.11	4.91	12.5	264	30.6	90.8	90.8	73.1	90.7	1.9	NIL
52	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.33	1.99	2.79	4.81	11.2	210	37.4	48.9	73.7	125.8	80.4	2.2	Target not Detected
53	Lamivudine	Zidovudine	Efavirenz	Septrin	Vitafol	4.84	2.24	2.08	4	9.8	295	41.3	61.6	60.4	164.8	80.7	6.83	<20
54	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	6.3	3.24	2.81	4.15	11.9	138	40	12.9	20.3	78.4	100.9	4.1	31621
55	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.58	2.89	2.13	2.61	8.9	152	30.3	48.6	54.1	73.5	106.2	9.4	43237
56	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.73	2.97	2.73	4.13	11.4	415	42.1	49.5	60.7	120.2	99.5	10.3	207942
57	Lamivudine	Zidovudine	Nevirapine	Septrin	Vitafol	7.29	4.01	2.81	4.24	12.2	254	42.3	15.2	13.1	70.8	85.6	2.6	1958
58	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.44	2.39	2.75	4.16	10.8	200	27.6	49.7	44.5	96.3	115.1	9.8	NIL
59	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	5.73	2.13	2.03	3.38	8.1	189	43.2	32.3	45.5	92.7	94.8	4.1	153107
60	Lamivudine	Tenofovir	Efavirenz	Septrin	Vitafol	6.14	2.38	2.59	4.96	12.5	189	51.7	23.6	22.5	136.3	106.7	8.8	56
61	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Septrin	Vitafol	3.39	2.92	3.11	4.18	11.9	179	28.5	60.3	72.4	81.5	84.5	4.12	961516
62	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Septrin	Vitafol	53.91	4.01	1.62	3.98	9.7	161	41.9	30.5	32.7	54.3	95.6	2	Target not Detected
63	Lamivudine	Efavirenz	Tenofovir	Septrin	Vitafol	6.55	4.02	2.1	3.14	9.14	289	34.3	35.9	38.2	74.6	83	2.71	17319
64	Lamivudine	Zidovudine	Nevirapine 200mg	Septrin	Ferroglobin capsules	4.35	1.54	2.31	2.66	8.1	311	26	35	59	110	60	8.5	37205

65	5Lamivudine	Efavirenz	Tenofovir	Septrin	Vitafol	6.15	4.24	1.2	4.18	8.6	202	29.6	20.1	28.9	123.4	84.1	10.9	2103
66	Lamivudine	Efavirenz	Tenofovir	Septrin	Vitafol	5.84	3.81	2.28	4.86	12.3	398	35.3	42.2	48.5	85.6	90.4	2.8	307940
67	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Septrin	Vitafol	5.94	3.58	2.1	4.92	12.5	379	46.4	43.2	48.3	128.2	81.8	8.5	NIL
68	Lamivudine	Tenofovir	Efavirenz 600mg	Septrin	Vitafol	6.67	4.01	2.08	3.28	11.7	135	32.8	4.2	28.6	101.4	105.8	2.13	197
69	Nevirapine	Lamivudine	Zidovudine	Septrin	Vitafol	5.58	1.75	3.09	2.96	12.3	266	50.2	21.8	29.3	154.6	88.1	4.74	Target not Detected
70	Nevirapine	Lamivudine	Zidovudine	Septrin	Vitafol	3.05	1.64	1.06	4.32	14.2	143	45	15.5	28.7	93.2	96.4	2.85	463873

ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads (Copies/mL)
71	Lamivudine 150mg	Zidovudine 300mg	Nevirapine 200mg	Amlodipine	Vitafol	4.2	1.36	2.06	3.87	12	195	45.2	13	28	135.7	93.6	8.62	
72	Zidovudine 300mg	Lamivudine 300mg	Efavirenz 600mg	Septrin	Vitafol	4.57	2.19	1.83	3.57	11.1	114	52.8	23.4	37.6	67	97.4	4.05	
73	Lamivudine 150mg	Tenofovir	Efavirenz 600mg	Amlodipine	Vitafol	2.54	1.02	0.91	6.67	25.7	35	49.6	12.9	20.7	129.7	101.4	6.33	
74	Zidovudine	Lamivudine	Efavirenz 600mg	Flaggy	Triple Action	2.84	0.9	1.57	5.32	14.3	199	49	5.7	21.1	150.5	85.7	3.88	Target not Detec
75	Zidovudine	Lamivudine	NVP Nevirapine	Arthermeter	Lumenfantrin	6.63	2.47	2.65	4.03	9.8	270	44.2	8.5	28.1	132	101.7	3.92	
76	Zidovudine	Lamivudine	EFV Efavirenz	Septrin	Vitafol	5.06	1.96	2.48	3.49	12.2	311	49.1	10.5	20.9	85	80.2	3.3	12
77	Zidovudine	Lamivudine	EFV Efavirenz	Septrin	Vitafol	5.99	2.43	2.92	4.07	13.8	303	50.2	13.1	30.4	124.7	99.5	3.7	<20
78	Zidovudine	Lamivudine	EFV Efavirenz	Septrin	Vitafol	6.32	1.46	3.8	4.35	12	293	49.1	8.8	22.7	130.1	99.9	3.38	
79	Zidovudine	Lamivudine	EFV Efavirenz	Septrin	Vitafol	6.4	2.25	3.45	3.47	12.6	201	45.8	10.7	20.1	130	105.6	5.72	
80	Zidovudine	Lamivudine	Efavirenz	Septrin	Vitafol	4.65	1.5	2.2	4.21	11.4	261	32.1	98.3	250	111.6	107.7	3.9	4
81	Zidovudine	Lamivudine	Nevirapine	Septrin	Vitafol	6.49	2.92	2.9	3.59	12.8	397.4	28.8	100.8	106.5	52.1	90.5	5.54	
82	Lamivudine	Tenofovir	Efavirenz 600mg	Septrin	Zingovite	2.44	1.56	0.49	1.78	6.5	197	42.5	31.4	47.7	91.5	114.7	4.36	4
83	Lamivudine	Tenofovir	Efavirenz 600mg	Septrin	Vitafol	6.23	1.45	4.02	6.47	22.1	64	52.3	25.4	24.1	86	100.1	2.46	1
84	Lamivudine	Tenofovir	Efavirenz 600mg	Septrin	Vitafol	2.05	0.66	0.82	7.26	25.9	49	46.9	46.4	43.1	84.2	109	3.87	
85	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Septrin	Vitafol	6.83	4.14	2.03	2.11	10.4	250	45.1	20.4	36.5	67.3	86.2	1.98	
86	Tenofovir	Lamivudine	Efavirenz 600mg	Septrin	Vitafol	4.6	1.61	2.4	3.58	13.5	224	46.6	37	29.8	69	90.9	2.52	
87	Tenofovir	Lamivudine	Efavirenz 600mg	Septrin	Danwell syrup	5.17	1.4	3.19	2.06	9.1	236	49.5	17	23.4	87.4	91.9	2.57	
88	Emtricitabine 200mg	Tenofovir 300mg	Efavirenz 600mg	Metformin Denk 500mg	Zingovite	3.76	1.88	1.37	7.53	23.8	61	46.4	17	18.3	68.8	95.1	3.64	
89	Emtricitabine 200mg	Tenofovir 300mg	Efavirenz 600mg	Septrin	Vitafol	3.86	1.54	1.66	3.5	10.7	310	45.6	19.8	24.3	80.6	102.4	4.15	
90	Emtricitabine 200mg	Tenofovir 300mg	Efavirenz 600mg	eye drop	Gentamycin eye drop	4.38	2.08	1.7	4.17	11.9	218	463.6	40.3	34.8	88.9	88.8	3.14	
91	Emtricitabine 200mg	Tenofovir 300mg	Nevirapine 200mg	Vitafol	Septrin	5.62	2.49	2.15	3.76	11.4	312	48.9	17	27.2	77.5	104.4	2.46	
92	Emtricitabine 200mg	Tenofovir 300mg	Nevirapine 200mg	Septrin	Vitafol	3.53	94	2.24	2.88	9.8	101	45.7	28.7	20.1	74.3	86.6	5.12	Target not Detec
93	Tenofovir Disoproxil	Lamivudine 300mg	Efavirenz 600mg	Doxycycline 100mg	Vitafol	4.27	1.51	2.24	3.6	12.9	242	49.9	19.7	34.5	73.5	96	4.8	
94	Emtricitabine 200mg	Tenofovir 300mg	Nevirapine 200mg	Vitafol	Septrin	6.96	1.56	4.74	5.63	17.5	178	45	44.1	40.8	126.7	103.3	4.71	

95	Tenofovir Disoproxil	Lamivudine 300mg	Efavirenz 600mg	Vitafol	Septrin	5.34	2.46	2.25	4.33	17.2	148	46.9	14.6	13.7	81.8	104.1	4.21	
96	Tenofovir Disoproxil	Lamivudine 300mg	Efavirenz 600mg	Amlodipine 10mg	Zingovite	3.04	1.61	1.07	6.69	22.3	94	49.1	15.1	22.4	86.9	95.7	4.11	
97	Tenofovir Disoproxil	Lamivudine 300mg	Efavirenz 600mg	Septrin	Vitafol	2.85	0.2	1.7	4.33	13	248	51.4	51.3	31.6	100.3	99.9	7.2	1
98	Tenofovir 300 mg	Emtricitabine 200mg	Efavirenz 600mg		Vitafol	4	1.31	2.36	4.68	16.9	205	50.8	69.9	50.9	60	103.3	2.68	
99	Lamivudine	Zidovudine 300mg	Nevirapine 200mg		Vitafol	6.91	4.02	2.15	3.86	12.5	148	52.5	30.6	27.9	100.4	105.4	4.62	Target not Detec
100	Lamivudine 150mg	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	6.35	1.13	4.18	4.85	9.9	150	31	28.9	42.1	106.2	112.5	4.28	3
101	Tenofovir 300 mg	Lamivudine 300mg	Efavirenz 600mg	Vitafol	Septrin	5.3	2.89	1.95	4.97	12.9	215	51.4	39.9	26.9	96.5	100.3	3.64	Target not Detec
102	Tenofovir 300 mg	Lamivudine 300mg	Efavirenz 600mg	Elaronvite	Septrin	5.31	2.17	2.23	5.11	12.7	205	49.3	39.9	58.4	64.9	91.1	2.16	
103	Emtricitabine 200mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	5.86	3.19	2.11	4.28	11.3	289	44.7	21.5	32.3	35.8	106.7	3.12	
104	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	4.9	3.04	1.38	7.7	21.8	167	51.9	25	20.2	0	101.7	4.23	Target not Detec
105	Tenofovir 300mg	Efavirenz 600mg	Lamivudine 300mg	Vitafol	Septrin	4.65	1.11	2.05	7.8	22.3	529	52	21.5	23.3	56.9	89.3	3.14	

ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads (Copies/mL)
106	Lamivudine	Tenofovir 300 mg	Efavirenz 600mg	Vitafol	Septrin	5.51	2.14	2.01	9.32	18.3	511	47.1	32.2	33.4	41.4	92.2	2.83	Target not Detected
107	Emtricitabine 200mg	Tenofovir 300 mg	Efavirenz 600mg	Vitafol	Septrin	5.41	2.07	1.99	7.44	21.9	377	50.9	49.5	28.4	34.7	98	3.27	154
108	Lamivudine	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	7.14	3.02	2.75	7.8	22.4	491	52	36.3	31.3	37.9	98	3.05	1602
109	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	6.39	3.11	2.15	8.9	23.8	215	44	32.9	29.8	47.1	105.8	3.12	22
110	Lamivudine	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	6.96	2.93	3.04	7.36	23.1	320	50.9	16	21.5	47.5	102.8	3.02	112
111	Emtricitabine 200mg	Tenofovir 300mg	Nevirapine	Vitafol	Septrin	7.78	1.85	2.75	4.3	14	255	51.3	22.8	26.1	31.5	98.2	2.52	61
112	Zidovudine	Lamivudine	Nevirapine	Vitafol	Septrin	7.22	4.04	1.95	4.24	11.2	324	46.4	27.5	25.8	20.2	102.2	4.22	385
113	Emtriocitabine200mg	Tenofovir 300mg	Efavirenz 600mg			4.29	1.62	2.03	7.01	19.5	86	47.5	26.7	35.6	58.6	115.6	4.51	Target not Detected
114	Lamivudine	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	5.02	1.99	3.19	6.82	23	162	44.1	13.5	17.1	27.1	104.6	1.87	533
115	Lamivudine	Efavirenz 600mg	Tenofovir 600 mg	Vitafol	Septrin	4.92	1.62	1.89	3.36	13.3	280	37.6	56.8	47.3	105.1	77.7	3.67	89
116	Emtricitabine 200mg	Nevirapine	Tenofovir 300 mg	Vitafol	Septrin	4.87	2.41	2.12	6.21	21.5	97	42.1	10	20	212.4	112.4	6.54	38
117	Lamivudine	Efavirenz 600mg	Tenofovir 600 mg	Vitafol	Septrin	5.65	2.02	1.97	3.82	12.6	220	48.2	18.8	19.3	38.7	95.4	4.7	42
118	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	4.95	1.81	1.65	3.37	10.5	285	44.5	19.2	20.2	33.9	82	4.73	Target not Detected
119	Lamivudine	Efavirenz 600mg	Tenofovir	Lisinopril	Amlodipine	5.69	3.17	2.07	4.1	11.9	268	50.3	16.5	18.2	47.4	92.5	3.32	83
120	Lamivudine 150mg	Efavirenz 600mg	Zidovudine 300 mg	Vitafol	Septrin	9.32	2.91	4.83	5.58	17.2	73	46.6	32.8	23.9	46.7	109.1	3.85	225721
121	Lamivudine 150mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	4.72	1.58	2.02	4.36	12.7	337	44.8	27.3	19	87.1	94.1	1.89	Target not Detected
122	Lamivudine 300 mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	5.33	4.02	1.15	5.06	17.2	114	42.9	15.5	17.6	95.2	88.8	2.61	4209
123	Lamivudine 150mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	7.95	0.99	4.05	3.99	11.2	257	48.4	23.1	29.2	124.2	111.1	4.49	137832
124	Lamivudine 150mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	5.55	2.83	2.14	6.91	19.6	65	50.1	43.3	43.7	133.3	106.5	3.78	250
125	Lamivudine 150mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	5.66	2.97	1.97	5.48	17.7	129	32	14.8	12.7	66	75.5	3.12	6343
126	Lamivudine 300 mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	4.89	1.75	2.03	3.19	9.7	322	34	26.2	34.7	53.7	85.7	1.74	7372
127	Lamivudine 300mg	Efavirenz 600mg	Tenofovir 300 mg	Vitafol	Septrin	5.98	2.84	1.75	3.79	10.6	169	29.2	26.2	45.1	91.2	72.7	2.64	413
128	Lamivudine 150mg	Zidovudine 300mg	Nevirapine 200mg	Zingovite		5.73	1.91	2.07	3.66	10.3	133	35.9	25.3	30.5	68	85.9	2.69	34
129	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	6.9	2.53	3.02	4.03	12.5	81	40.3	11.1	16.5	112.2	72.6	2.88	27
130	Lamivudine 150mg	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	7.11	2.06	1.82	3.14	11.3	144	42.2	15.3	22.5	97.2	80.9	4.67	102
131	Lamivudine 150mg	Zidovudine 300mg	Efavirenz 600mg	Septrin		7.07	4.01	2.02	4.24	11.2	389	49.1	33.7	26	105.6	100.3	4.22	872

132	Emtricitabine 200mg	Nevirapine	Tenofovir	Vitafol	Septrin	5.89	2.72	2	3.45	11.7	216	51.4	35.4	24.4	136.3	95	4.26	146
133	Lamivudine 150mg	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	7.63	4	1.95	6.27	17.3	62	41	22.4	21.8	70	88.8	2.24	931
134	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	4.82	2.13	2.06	5.48	17.7	129	36.3	45.8	45	73.5	86.9	3.9	54
135	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	4.46	1.99	1.74	3.94	12.4	246	39.1	19.4	19.3	80.4	75.8	3.22	33
136	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Allergic to co-trimoxazole	4.36	1.08	2.65	3.95	12.2	259	33.2	10.7	13.3	47.1	68.5	2.85	Target not Detected
137	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	8.85	0.99	4.84	4.23	13.2	249	37.4	20	17.5	89.1	71.1	4.25	346021
138	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	3.95	0.38	2.01	4.51	12.5	223	38.7	20.8	20	47	75.7	3.12	Target not Detected
139	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	9.16	0.12	4.17	7.64	20.9	71	42.9	27.8	24.5	84.3	100	3.17	1767883
140	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	5	2.35	2.07	3.62	12.7	256	38.7	18.1	16.7	79.1	75.1	2.62	43

ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads (Copies/mL)
141	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	7.96	3.01	3.09	8.06	24	35	33.4	13.5	15	54.1	67.3	1.66	103948
142	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	4.11	2.03	1.55	4.82	14.3	131	41.5	13.4	23.5	43.6	90.6	4.01	61
143	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	3.54	2.01	1.13	5.07	17.2	114	38.5	19.2	20.6	65.6	83.8	3.19	<20
144	Lamivudine 300mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	4.21	1.75	2.19	4.18	14.4	139	32.4	12.7	15.1	65.8	58.4	2.77	638
145	Emtricitabine 200mg	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	4.48	2.84	1.15	4.27	12.9	173	36.2	24.5	21.3	90.6	65.3	2.31	<20
146	Lamivudine	Tenofovir 300mg	Efavirenz 600mg	Vitafol	Septrin	3.71	1.74	1.26	5.15	14.7	275	50.9	13.2	8.24	45.1	113.7	1.99	349864
147	Lamivudine	Nevirapine	Zidovudine 300 mg	Vitafol	Septrin	2.95	0.88	1.82	3.59	12.4	72	44.4	11.5	30.8	64.2	94.9	1.3	<20
148	Lamivudine	Nevirapine	Zidovudine 300 mg	Vitafol	Septrin	4.41	2.06	1.8	4.18	14.9	238	56.9	43.7	29.4	76.6	110.1	1.8	Target not Detected
149	Lamivudine	Efavirenz	Zidovudine 300 mg	Vitafol	Septrin	3.49	0.98	2.08	3.29	10.9	184	45.6	19.7	22.9	78.5	82.2	1.5	19500
150	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	4.89	1.33	2.42	3.33	11.8	171	51.9	20.1	9.2	78.4	125.2	1.3	24932
151	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	3.93	0.97	2.19	3.52	9.1	411	44.6	56	46.3	100.7	112.8	1.3	70115
152	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	6.85	3.97	2.2	3.19	9.9	300	43.8	10.8	16.8	30	87.4	2.7	121
153	Lamivudine	Nevirapine	Zidovudine 300 mg	Vitafol	Septrin	4.18	1.79	1.92	4.06	12.8	142	46.3	50	47.1	88.5	109.4	2.3	77
154	Lamivudine	Nevirapine	Zidovudine 300 mg	Vitafol	Septrin	4.14	1.38	2.12	4.3	13.2	195	56.6	52.8	41.2	71.6	110.3	3.8	<20
155	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	3.08	1	1.22	3.58	12.6	248	44.9	34.5	31.9	98.6	102.5	2.3	35870
156	Lamivudine	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	3.8	1.36	2.01	3.37	12.1	293	52.8	22	33.2	82.8	99.5	2.3	1937
157	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	4.79	1.68	2.57	3.46	11.8	287	52.7	25.8	30.8	47.8	107.7	1.2	Target not Detected
158	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	1.69	0.64	0.71	5.24	20.1	70	54.8	33.2	86.5	100.7	105.3	1.5	62124

159	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	3	1.06	1.53	3.22	11.7	197	50.3	58.8	47.8	92	94.7	2.1	2350
160	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	4.22	1.31	2.64	3.64	11.8	115	43.2	22.7	14.8	77.6	129.2	2.5	Target not Detected
161	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	3.08	1.21	1.43	3.56	12.1	172	45.2	47.2	32.9	91.9	89	2.1	<20
162	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	3.93	0.88	2.26	3.67	11.2	307	53.3	91.2	85.7	62.7	108.6	1.3	10640
163	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	6.09	1.87	3.56	3.21	12.5	269	52.6	11	29.9	49.9	112	1.1	1708
164	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	4.76	0.98	3.21	4.18	12.9	221	49.5	52.5	19.1	77.6	132.2	1.3	853620
165	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	3.91	1.18	2.15	3.84	12.7	134	49.9	28.9	43.6	84.1	110.7	5.3	Target not Detected
166	Lamivudine	Tenofovir	Zidovudine 300 mg	Vitafol	Septrin	5.18	1.6	2.92	3.61	13	183	49.8	39.8	55.9	73.6	99.9	1.7	100
167	Lamivudine	Tenofovir	Zidovudine 300 mg	Vitafol	Septrin	2.02	0.81	0.85	8.45	21.2	47	52	45.2	21.47	131.3	119.1	1.15	130
168	Lamivudine	Zidovudine	Efavirenz 600mg	Vitafol	Septrin	3	1.16	1.41	4.15	11.7	138	55.1	10.9	11.6	77.4	80.9	2.9	129
169	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	2.23	0.76	0.84	2.03	5.9	135	50.7	16.7	41.2	10.9	102.3	3.24	125
170	Lamivudine	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	5.65	2.45	2.42	3.78	11.4	248	58.4	75.7	4.32	90.8	104.1	3.09	87581
171	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	1.56	0.46	0.97	7.23	26.2	26	56.2	30.5	31.72	36.8	111.9	3.95	1602
172	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	3.42	1.52	1.32	4.32	13.2	247	50.2	25.2	15	81.6	85.1	4.1	21569
173	Lamivudine	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	4.18	1.56	2.12	3.89	13.2	220	49.7	8	55.38	89.8	91	2.51	Target not Detected
174	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	3.55	1.16	1.81	3.69	13	126	52.1	71.6	10.54	42.7	95.5	5.67	Target not Detected
175	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	4.12	1.81	2.03	3.37	11.6	178	47.9	104.8	34.6	29.6	106	2.93	Target not Detected
ID	DRUG 1	DRUG 2	DRUG 3	OH DRUG1	OH DRUG2	WBC	NEUT#	LYMP#	RBC	HB	PLT	ALB	ALT	AST	CRbi	PRTB	URSL	Viral Loads
																		(Copies/mL)
176	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	2.32	1.06	0.94	5.94	17.7	88	51	13.2	29.54	10.4	106.4	4.65	34
177	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	5.46	1.47	3.53	4.09	11.6	178	42.9	27.1	30.4	100.2	84.7	2.6	22593
178	Emtricitabine 200mg	Nevirapine	Tenofovir	Vitafol	Septrin	4.12	1.62	1.64	3.9	12.1	267	52.2	21.5	2.34	61.8	95.8	3.8	13808
179	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	2.96	0.59	1.83	3.82	14.1	186	10.9	85.3	44.64	54.6	109.5	2.64	Target not Detected
180	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	4.02	1.16	2.23	3.26	10	312	47.8	21.1	16.7	35.7	85.4	2.3	Target not Detected
181	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	5.43	3.3	1.32	2.33	8.4	557	43.7	48.4	40	49.7	101	1.97	<20
182	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	5.41	1.02	3.4	3.24	10.4	81	34.2	8.1	7.84	70.4	109.5	2.99	Target not Detected
183	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	3.58	1.71	1.13	4.33	12.3	236	56.9	12.9	48.41	51.6	132.1	2.81	16715
184	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	7.03	2.93	3.32	3.81	13.5	315	46.4	23.2	12.5	89.1	88.9	3	84
185	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	5.89	3.05	2.14	3.49	12.1	152	57.7	18	10.08	65	126.7	4.67	352716
186	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	3.4	1.43	1.37	3.16	10	323	49.3	16.4	17.2	52.8	93.3	52.8	25
187	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	6.45	1.71	4.1	3.85	10	154	90.5	18	22.02	40.1	110.4	3.14	189

188	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	4.94	2.39	1.87	3.46	12.5	315	52.3	23.3	34.43	50.6	104.2	2.99	1260
189	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	4.54	1.71	2.22	3.33	11.1	280	48.4	14.9	20.5	81.8	97.1	3.5	<20
190	Lamivudine	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	4.32	2.18	1.73	4.71	13.2	75	46.2	34.8	78.7	63.2	103.2	3.1	238
191	Emtricitabine 200mg	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	4.21	1.37	2.31	2.83	10.3	211	57.3	24	20.07	63	102.3	2.74	115
192	Emtricitabine 200mg	Nevirapine	Efavirenz 600mg	Vitafol	Septrin	3.15	0.81	1.77	2.52	9.5	80	50.4	30.5	47.7	34.2	102.1	2.3	23
193	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	3.45	1.85	1.04	3.48	11.2	297	50.7	57	68.08	57.3	105.8	3.13	493
194	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	1.95	1.01	0.74	1.54	6.1	17	47.3	30.4	22.3	50.3	86.1	3.2	<20
195	Emtricitabine 200mg	Tenofovir	Nevirapine 200mg	Vitafol	Septrin	4.82	1.59	2.53	4.07	12.5	368	46.3	44.3	32.4	27.5	81	2.4	1034751
196	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	5.35	2.98	1.81	3.76	9.7	315	39.7	25.3	71.8	73.6	113.4	2.29	81830
197	Lamivudine	Zidovudine 300mg	Nevirapine 200mg	Vitafol	Septrin	6.08	2.64	2.07	3.69	10.1	215	64.1	19.3	23.4	77.5	110.1	1.53	<20
198	Lamivudine	Tenofovir	Efavirenz 600mg	Ferroglobin Capsules	Septrin	5.75	3.04	2.01	3.91	12.1	143	35	40.5	126.7	110.2	89.1	8.13	101675
199	Lamivudine	Tenofovir	Efavirenz 600mg	Vitafol	Septrin	5.62	2.56	2.51	4.39	11.5	347	32.5	21.9	32.6	64.9	100.1	3.1	Target not Detected
200	Lamivudine	Zidovudine 300mg	Efavirenz 600mg	Vitafol	Septrin	5.19	2.68	2.02	4.31	12.6	300	49.2	21.3	32.8	84.7	137.9	4.41	140

KEYS: WBC-White Blood cells, RBC- Red Blood cells, HB- Haemoglobin, PLT- Platelet count, ALB- Albumin, ALT- Alanine transaminase, AST- Aspartate aminotransferance, ALP-Alkaline phosphatase, CRbi- Creatinine, PRTB- Total Protein, URSL- Urea, OH- Others, NEUT#-Absolute Neutrophils, LYMP#- Absolute Lymphocytes.

APPENDIX II

1.0. **BASIC INFORMATION**

1.1 Participant's Name….. **NAME**

1.2 **SEX**

1.3 Age (Complete years)..... **AGE**

Sex……

….

1.5 Date of **DATVIS** Interview:.....……..…

2.0 SOCIO-DEMOGRAPHIC CHARACTERISTICS

2.1 What is your marital status?

Married	Not Married	Divorced	**MARRY**

2.2 What is your highest level of education?

1. None	2. Primary	3. Middle/JSS	4. Technical/SSS	**EDU**
5. Tertiary				

1.3 Economic status: Low, Medium, High

Low: (50gh-500gh)	Medium: (600gh-1600gh)	1700gh-3000gh

2.4 What is your religion?

1.Christian	2.Muslim	others

RELIGION

1. MEDICAL HISTORY

3.1. HIV status…… **HIV**

1. Yes	2. No

3.2. If 'Yes' since when…….…… **HIVDT**

3.3. Are you on the HAART therapy?..... **HAART**

1. Yes	2. No

3.4. What drugs are they?... **DRUGS**

3.5. Do you have any other medical conditions such as:……

1.	Diabetes	1. Yes	2. No
2.	Hypertension	1. Yes	2. No
3.	Kidney problem	1. Yes	2. No
4.	Liver problem	1. Yes	2. No
5.		1. Yes	2. No

3.6 If 'Yes', for Question 5, do you take any therapy for such **MEDICA** medical conditions? **L**

1. Yes	2. No

3.7. If 'Yes', is it orthodox or **HIV** herbal?.....…….

1. Orthodox	2. Herbal

3.8. Name of drug or herbal product if **HIV** available?…

3.9. Are you taking any drug or herbal **HIV** product?.....……

1. Yes	2. No

3.10. Category of **HIV** drug?.....…….

1.Blood tonic	2. Antibiotics
3. Antipyretics	4. Stimulants
5. Other……	

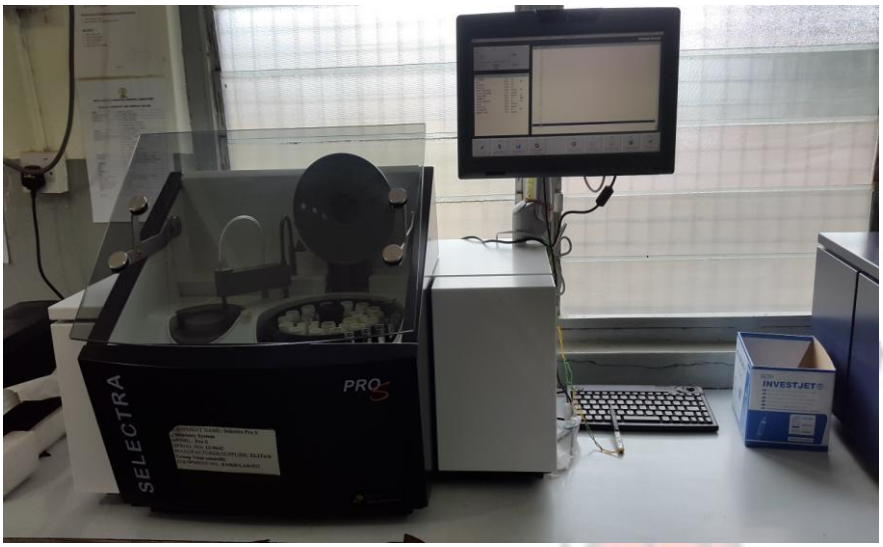
Interviewer's **CODE**

Code…….....

CHECK THE FORM TO ENSURE THAT ALL SECTIONS HAVE BEEN COMPLETED APPROPRIATELY

APENDIX III

The Sysmex XS *(XS-100i/ XS-500i)* Automated Haematology Analyser



The Selectra ProS Automated chemistry analyser

COBAS TaqMan HIV-1 Qual Machine

COBAS AmpliPrep HIV-1 Qual Machine

COBAS Thermomixer Machine

APPENDIX IV

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICAL SCIENCES / KOMFO ANOKYE TEACHING HOSPITAL

COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Our Ref: CHRPE/AP/023/15

20th January, 2015.

Dr. Theophilus Ben Kwofie
Department of Clinical Microbiology
School of Medical Sciences
KNUST-KUMASI.

Dear Sir,

LETTER OF APPROVAL

Protocol Title *"Determination of Hematological and Biochemical Abnormalities in HIV/AIDS Infected Patients Receiving Highly Active Antiretroviral Therapy at the Effia Nkwanta Regional Hospital in the Western Region."*

Proposed Site: *Effia Nkwanta Regional Hospital, HIV/AIDS Unit, Sekondi Takoradi, Western Region.*

Sponsor: *Principal Investigator.*

Your submission to the Committee on Human Research, Publications and Ethics on the above named protocol refers.

The Committee reviewed the following documents:

- A notification letter of 9th December, 2014 from the Effia Nkwanta Regional Hospital (study site) indicating approval for the conduct of the study in the Hospital.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Proposal.
- Questionnaire.

The Committee has considered the ethical merit of your submission and approved the protocol. The approval is for a fixed period of one year, renewable annually thereafter. The Committee may however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee should be notified of the actual start date of the project and would expect a report on your study, annually or at close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Thank you Sir, for your application.

Yours faithfully,

Rev. Prof. John Appiah-Poku
Honorary Secretary
FOR: CHAIRMAN

Room 7 Block J, School of Medical Sciences, KNUST, University Post Office, Kumasi, Ghana
Phone: +233 3220 63248 Mobile: +233 20 5453785 Email: chrpe.knust.kath@gmail.com / chrpe@knust.edu.gh