KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY,

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COLLEGE OF HEALTH SCIENCES

FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

DEPARTMENT OF CLINICAL AND SOCIAL PHARMACY

PREVALENCE & CAUSES OF ANTIRETROVIRAL TREATMENT FAILURE AMONG ADULTS RECEIVING THERAPY AT KOMFO ANOKYE TEACHING HOSPITAL

BY

RAPHAEL KWEKU OBENG (REV.)

B. PHARM. (HONS)

FEBRUARY, 2010

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A THESIS SUBMITTED TO THE DEPARTMENT OF CLINICAL AND SOCIAL PHARMACY, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

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DEDICATION

I dedicate this work to the glory of the Most High God, to all persons living with HIV/AIDS and to all stakeholders in the fight against this condition.

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My very good friend Mr. Joseph Attakorah of KATH deserves special recognition for his role in securing my admission to this programme in my absence. Lastly, my wife Julie, Kobby, Akua, Kweku and Kobina, our children whose comfort I often denied for the sake of this project, deserve commendation for their prayer support, patience and tolerance.

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.

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Supervisor's Name Signature Date

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Head of Dept. Name Signature Date

ABSTRACT

Background: Antiretroviral therapy (ART) program at Komfo Anokye Teaching Hospital began in February 2004 with Six (6) patients. As at April 2009, a little over four thousand two hundred (4,200) people had been offered antiretroviral drugs cumulatively. Whereas a significant number of the patients are responding very well to treatment, others have experienced treatment failure on first line regimen and subsequently been switched to second line regimen. The aim of the study was to investigate the prevalence of antiretroviral treatment failure among adults at Komfo Anokye Teaching Hospital.

Method: The study was retrospective, organized in two phases. The first phase was designed to examine patients' folders and to collect data relevant to the topic under study. The second phase involved personal interviews of patients who satisfied the requirements of participating in the study. For the purpose of the first phase a data collection tool (appendix 1) was designed and used.

Results: The prevalence of antiretroviral treatment failure among adult patients attending clinic at Komfo Anokye Teaching Hospital was found to be approximately 3.7%. More than 50% of the study population experienced failure by the end of their tenth month after treatment initiation. Some 14% of the study participants demonstrated no positive immunological response to initiation/continuation therapy.

Conclusion: Poor adherence to treatment was found to be a possible factor contributing to treatment failure. Underpinning this were financial and resource constraints. Previous exposure to antiretroviral medicines was not found to be a direct cause of treatment failure in this study but the result is suggestive.

LIST OF ACRONYMS

ABC	Abacavir
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy
AZT/ZDV	Azidothymidine/zidovudine
CD4	Cluster of Differentiation
DDI	Didanosine
D4T	Stavudine
HIV	Human Immunodeficiency Virus
EFV	Efavirenz
LPV/r	Lopinavir/ritonavir
NACP	National AIDS Control Program
NRTI	nucleoside reverse transcriptase inhibitor
NNRTI	Non nucleoside reverse transcriptase inhitor
NVP	Nevirapine
PI	Protease inhibitor
PMTCT	Prevention of mother-to-child transmission
3TC	Lamivudine
TDR	Transmitted Drug Resistance
VCT	Voluntary counseling and testing
WHO	World Health Organization

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CHAPTER ONE

INTRODUCTION

1.1 EPIDEMIOLOGY

Since the early 1980's the world has experienced a condition that has proved to be difficult to handle. The history behind this condition is that in June 1981, five cases of a type of pneumonia known as *Pneumocystis carinii* (now *Pneumocystis jiroveci*) infection were described among homosexual men in the USA. Other unusual conditions such as Kaposi's sarcoma (KS), a type of cancer were reported shortly afterwards. It was discovered that in each of these patients, there was a significant impairment of cellular immune response. This therefore gave rise to the term acquired immune deficiency Syndrome (AIDS) [1]

In 1984, a new retrovirus later named human immunodeficiency virus (HIV) was isolated and implicated as the cause of AIDS. The condition soon spread and was identified among other population groups such as intravenous drug users and hemophiliacs. As the epidemic continued to grow, a strong relationship between transmission and heterosexual intercourse as well mother-to-child was strongly established. Reports of its occurrence in other countries were increasingly received. [1]

In the developing world (particularly Sub-Saharan Africa, South-East Asia, and South America), numbers continued to increase alarmingly with prevalence rates up to 40-50% reported in communities like Botswana and South Africa. The global statistics released in 2007 indicate that out of the world's population of about 6.7 billion, some

33 million people were living with HIV/AIDS and that women aged fifteen years and more constituted 15.5 million of the cases. AIDS related deaths and children with HIV/AIDS constituted 2 million each. Lastly, the report also revealed that adult HIV prevalence stands at 0.8% [2]

1.2 HIV/AIDS IN GHANA

The first case of AIDS was identified in Ghana in 1986. Since then there have been many developments in response to the epidemic. These include the redefinition of the continuum of prevention and care that recognizes the role of antiretroviral therapy (ART) in the care and support of persons living with HIV/AIDS [3]

Since the first case was identified, more cases have been reported but prevalence values have been fluctuating over the years. In 2007, the estimated adult national HIV prevalence was 1.9% with an estimated 264,481 persons living with HIV and AIDS. This is made up of 153,851 females and 110,666 males giving a female: male ratio of 1.4:1. In the same year, there were 16,947 children living with HIV and an estimated 2,959 babies were born to HIV positive mothers. The cumulative AIDS deaths were estimated at 180,899. Sexual spread still remains the main mode of transmission accounting for an estimated 80% of all cases. Mother-to-child (vertical) transmission accounts for 15% while blood and blood products take about 5%. [4]

The 2007 HIV Sentinel Survey (HSS) gave the median prevalence of HIV among antenatal clinic clients as 2.6%. Two major age groups were most affected. These are 25-29 and 35-39 year olds. Each had prevalence of 3.5%. The survey additionally

reported that both HIV 1 and 2 are found among the Ghanaian population. HIV 1 is the predominant type accounting for about 96.8%. The prevalence of HIV 2 on the other hand is 1.4% while HIV 1 & 2 dual infection is estimated as 1.8%. [4]

1.3 SOCIO-ECONOMIC IMPACT OF HIV/AIDS

Data in support of socio economic impact of HIV/AIDS locally could not be accessed. However, a critical evaluation of the situation indicates that HIV/AIDS impacts heavily on almost all aspects of the socio-economic life of Ghana as a country. A publication cited on the internet which is attributed to an international AIDS charity organization known as AVERT summarizes the HIV/AIDS burden on Sub Saharan Africa (Table 1.1). It indicates that an estimated 22 million adults and children were living with HIV as at the end of the year 2007. During that year, an estimated 1.5 million Africans died of AIDS. The epidemic left some 11.6 million orphaned African Children [5]. With particular reference to Ghana 260,000 adults aged 15 years and above were living with the virus. Women constituted 150,000 and children 17,000. There were 21,000 AIDS related deaths which resulted in 160,000 orphaned children. The situation as pertains in the other countries within the region is summarized in the table below.

Table 1.1: HIV/AIDS burden on Sub-Sahara African Countries

Country	People living with HIV/AIDS	Adult (15-49) rate %	Women with HIV/AIDS	Children with HIV/AIDS	AIDS deaths	Orphans due to AIDS
Angola	190,000	2.1	110,000	17,000	11,000	50,000
Benin	64,000	1.2	37,000	5,400	3,300	29,000
Botswana	300,000	23.9	170,000	15,000	11,000	95,000
Burkina Faso	130,000	1.6	61,000	10,000	9,200	100,000
Burundi	110,000	2.0	53,000	15,000	11,000	120,000
Cameroon	540,000	5.1	300,000	45,000	39,000	300,000
Central African Republic	160,000	6.3	91,000	14,000	11,000	72,000
Chad	200,000	3.5	110,000	19,000	14,000	85,000
Comoros	<200	<0.1	<100	<100	<100	<100
Congo	120,000	3.5	43,000	6,600	6,400	69,000
Côte d'Ivoire	480,000	3.9	250,000	52,000	38,000	420,000
Dem. Republic of Congo	400,000-500,000	1.2-1.5	210,000-270,000	37,000-52,000	24,000-34,000	270,000-380,000
Djibouti	16,000	3.1	8,700	1,100	1,100	5,200
Equatorial Guinea	11,000	3.4	5,900	<1,000	<1,000	4,800
Eritrea	38,000	1.3	21,000	3,100	2,600	18,000
Ethiopia	980,000	2.1	530,000	92,000	67,000	650,000
Gabon	49,000	5.9	27,000	2,300	2,300	18,000
Gambia	8,200	0.9	4,500	<1,000	<1,000	2,700
Ghana	260,000	1.9	150,000	17,000	21,000	160,000
Guinea	87,000	1.6	48,000	6,300	4,500	25,000
Guinea-Bissau	16,000	1.8	8,700	1,500	1,100	6,200
Kenya	1,500,000 2,000,000	7.1-8.5	800,000-1,100,000	130,000-180,000	85,000-130,000	990,000-1,400,000
Lesotho	270,000	23.2	150,000	12,000	18,000	110,000
Liberia	35,000	1.7	19,000	3,100	2,300	15,000
Madagascar	14,000	0.1	3,400	<500	<1,000	3,400
Malawi	930,000	11.9	490,000	91,000	68,000	560,000
Mali	100,000	1.5	56,000	9,400	5,800	44,000

Mauritania	14,000	0.8	3,900	<500	<1,000	3,000
Mauritius	13,000	1.7	3,800	<100	<1,000	<500
Mozambique	1,500,000	12.5	810,000	100,000	81,000	400,000
Namibia	200,000	15.3	110,000	14,000	5,100	66,000
Niger	60,000	0.8	17,000	3,200	4,000	25,000
Nigeria	2,600,000	3.1	1,400,000	220,000	170,000	1,200,000
Rwanda	150,000	2.8	78,000	19,000	7,800	220,000
Senegal	67,000	1.0	38,000	3,100	1,800	8,400
Sierra Leone	55,000	1.7	30,000	4,000	3,300	16,000
Somalia	24,000	0.5	6,700	<1,000	1,600	8,800
South Africa	5,700,000	18.1	3,200,000	280,000	350,000	1,400,000
Swaziland	190,000	26.1	100,000	15,000	10,000	56,000
Togo	130,000	3.3	69,000	10,000	9,100	68,000
Uganda	1,000,000	6.7	520,000	110,000	91,000	1,000,000
United Rep. of Tanzania	940,000	5.4	480,000	130,000	77,000	1,200,000
Zambia	1,100,000	15.2	560,000	95,000	56,000	600,000
Zimbabwe	1,300,000	15.3	680,000	120,000	140,000	1,000,000
Total sub-Saharan Africa	22,000,000	5.0	12,000,000	1,800,000	1,500,000	11,600,000

With such a heavy burden, one can conjecture that a significant proportion of the vibrant workforce of the productive sector was lost to AIDS. In addition to losses due to deaths, government in collaboration with other stakeholders spends huge sums of money that would have otherwise been channeled to other sectors of the economy in providing both human and material resources to offer care to persons living with HIV/AIDS. Productive hours are lost in organizing funerals for the departed ones. Family members spend scarce financial resources that could have gone into feeding young children and giving them good education rather on funeral arrangements. All

these and many more that cannot be mentioned readily are some of the impacts on the nation.

1.4 NATIONAL INTERVENTION STRATEGIES

In order to mitigate the impact of HIV/AIDS epidemic on the socio-economic life of the people of Ghana, the government through the Ministry of Health and its agencies designed various interventions by way of responding to the situation. The response to the epidemic included priority interventions which initially focused on promotion of safe sex, condom use, improved management of sexually transmitted diseases (STDs), safe blood transfusion, infection control, nursing/clinical care and counseling. Others are home based care and prevention of mother-to-child transmission. [6]

The purpose of these intervention strategies were to reduce the number of new infections and to improve the quality of life of persons living with HIV and AIDS. For this reason Government of Ghana through its agencies and partners initiated antiretroviral therapy (ART) program in June 2003 on pilot basis at two sites in the Manya Krobo district of the Eastern region. The pilot project was extended to Korlebu and Komfo Anokye Teaching Hospitals in Accra and Kumasi respectively.

Since then it has been the agenda of government to expand access to comprehensive care to other sites in the country using lessons drawn from the pilot project. By December 2004, a total of 2,017 adults and children had accessed treatment from the four pilot sites. As at September 2008, over 90 health facilities were offering

antiretroviral therapy (ART) and related services. By the end of 2007, the cumulative number of persons living with HIV initiated on ART had exceeded 13,000. By way of responding to the call for universal access to treatment, care and support for PLHIV, the national goal was to put 70,000 PLHIV on ART by the year 2010.

In order for these programmess to run effectively, various bodies were established and charged with specific functions in the general context of addressing the HIV/AIDS scourge. Government of Ghana provided a framework for policy direction and strategy in the late 1980's [6]. The epidemic was managed initially as a disease but not a developmental issue hence the national response was medically oriented. The National Advisory Commission was established in 1985 to advise Government on HIV/AIDS Issues. The National AIDS Control Program (NACP) was also established in 1987 within the Ministry of Health and given the mandate of implementing and coordinating HIV/AIDS programs. A national HIV/AIDS/STI's policy document was initiated and finally developed.

Later on the need for a multidimensional approach to handling HIV/AIDS issues was realized. This then led to the establishment of the Ghana AIDS Commission in 2001 by a Cabinet decision to serve as a supra ministerial body. It also led to the involvement of ministries, departments, and agencies (MDAs), Civil Society Organizations (CSOs), Non Governmental Organizations (NGOs), Community Based Organizations (CBOs) and Faith Based Organizations (FBOs). A very essential component of the programme has been private sector participation which has been helping to reach more sections of

society. In all these efforts, the Ministry of Health through NACP acts as the lead technical agency for the Ghana AIDS Commission (GAC).

The Ghana AIDS Commission as a supra ministerial body is specifically mandated to carry out the following functions in the prevention and control of HIV/AIDS in Ghana

- Formulating national policies and strategies
- Providing high-level advocacy for HIV/AIDS prevention and control
- Providing effective leadership in the national planning of programmes
- Expanding and coordinating the national response
- Mobilizing, managing resources and monitoring their allocation and utilization
- Fostering linkages and networking among stake holders.

Assessing the government policy response to HIV/AIDS in Ghana, Fobil and Soyiri have indicated that there has been considerable political commitment both in the past and present, and Government has moved to operationalise the National Strategic Framework through multi-sector collaboration[7]

1.5 ANTIRETROVIRAL THERAPY PROGRAMME AT KOMFO ANOKYE TEACHING HOSPITAL (KATH)

Komfo Anokye Teaching Hospital is one of four sites chosen throughout Ghana to offer antiretroviral therapy (ART) to persons living with HIV/AIDS on a pilot basis. Since the programme began in February 2004, information received from HIV/AIDS data clerks at KATH indicate that about 9,760 patients (3,139 males and 6,631 females)

have been registered as at the end of April 2009. Out of this number, about 4,232 (1,455 male and 2,777 females) representing (43%) have benefited from ART, with the rest 5,528 (57%) also benefiting from management of opportunistic infections on regular basis while waiting to be put on antiretroviral medicines. Though a very significant number of the patients are still on their first line regimen, a few others have experienced treatment failure and have probably deteriorated and died or been switched to second line regimen. Since the start of the programme, an average of 70 new patients has been offered antiretroviral medicines monthly in addition to existing numbers. In either the registered or those on ART, the female to male ratio is approximately 2:1.

Before the program began in 2004 series of training workshops were organized for KATH staff for the purpose of building their capacity in order to be able to offer a comprehensive HIV/AIDS care to persons living with the disease. The multidisciplinary approach to the management of the condition necessitated the training of health workers with different professional backgrounds. These included counselors, laboratory scientists, nurses, doctors, pharmacists, data managers and social workers. The training programs were organized through collaborative efforts of the National AIDS Control Program (NACP), Family Health International (FHI) and other stakeholders.

Again, the multidimensional nature of care warranted interdepartmental collaboration within the hospital. Though, enrolment for ART takes place in the Directorate of Medicine, counseling and testing takes place in Polyclinic Directorate. Prevention of

mother to child transmission is handled at the antenatal clinic within the Directorate of Obstetrics and Gynecology. All these activities are well coordinated and reported periodically to a coordinator who in turn submits these reports to the appropriate stakeholders.

1.6 BACKGROUND AND PURPOSE OF THE STUDY

The driving force that informed the need to undertake this study bothers primarily on personal concerns about treatment outcomes and patients' behavior of adhering to therapy which ultimately impacts on such outcomes. Observation made at the clinic's pharmacy reveals that adherence to ART is gradually becoming a major challenge to the success of the ART programme at KATH. Secondly there is the perception that quite a significant number of the patients received some kind of therapies either in private medical facilities or took ARVs at home without any monitoring before continuation of therapy at KATH. Thirdly there is another perception that ARV drug shortages experienced in the country in the year 2005, as a result of which some patients experienced treatment interruption may, to some extent be linked to the current state of affairs regarding treatment failure. It is also believed that some patients perhaps relied on herbal treatments either for their opportunistic infections or as a result of claims by herbalists to provide complete cure of HIV/AIDS. It is therefore important for such perceptions to be investigated in order to see if there is indeed any meaningful correlation between such perceived cases and treatment failure.

Currently, with no cure in sight and with the problem of limited choice and availability of antiretroviral medicines, particularly in a resource-constrained setting like Ghana, the questions this research seeks to answer are: What is the prevalence of antiretroviral treatment failure among HIV/AIDS patients receiving care at KATH? What are the causes of the failure, and how can these be addressed? Seeking and providing answers to these questions is crucial in order to help patients receive optimum benefit from ART such that viral replication which is the biggest problem associated with HIV/AIDS will receive durable suppression with initial first line regimen. Those that have already been put on second line regimen will also be monitored more closely and given the needed assistance to adhere to treatment. This is particularly important in the sense that failure on second line regimen poses enormous challenges on clinical staff, family members of the infected and the national budget. Already, I am acquainted with the sad stories of two pediatric patients who have died as a result of failing on second line regimen, with others gradually moving towards the grave. Some adult patients have suffered similar fates.

1.7 AIM AND OBJECTIVES

The aim of the study was to investigate the prevalence of antiretroviral treatment failure among adults receiving therapy at Komfo Anokye Teaching Hospital.

From this aim five specific objectives were set. These are:

1. To describe the demographic characteristics of the patients who participated in the study.

2. To determine the prevalence of antiretroviral treatment failure among adult patients receiving therapy at Komfo Anokye Teaching Hospital.
3. To be able to estimate the mean time in months after treatment initiation when failure begins to occur.
4. To investigate the causes of antiretroviral treatment failure among patients receiving therapy at Komfo Anokye Teaching Hospital.
5. To make recommendations based on the findings of the study so as to assist in shaping clinical practice.

CHAPTER TWO

LITERATURE REVIEW

2.1 LIFE CYCLE OF HIV

In order to understand the life cycle of HIV, it is important first of all to be fairly acquainted with the structure of the virus. It is a proven scientific fact that HIV in common with other retroviruses possesses the enzyme reverse transcriptase and consists of a lipid bi-layer membrane surrounding the capsid (fig.2.1). It also has a surface glycoprotein molecule (gp.120) which has a strong affinity for CD4 receptor protein found predominantly in T helper/inducer lymphocytes. Monocytes and macrophages also have the probability of possessing CD4 receptors and can therefore become points of entry for HIV.

Scientific knowledge has shown that the process of HIV entry is more complex than originally thought to be and that in addition to CD4 attachment, subsequent binding to co-receptors such as CCR-5, CCR-2 or CXCR-4 and membrane fusion occur[8]. After penetrating the host cell, the virus sheds its outer coat and releases its genetic material using the reverse transcriptase enzyme. The viral RNA is then converted to DNA using nucleosides (fig.2.2). The enzyme that mediates this process is reverse transcriptase. The viral DNA is then integrated into the host genome in the cell nucleus, a process also mediated by the enzyme integrase. It then undergoes transcription and translation enabling the production of new viral proteins. The new viral particles are then

assembled and bud out of the host cells, finally maturing into infectious virions under the influence of protease or proteinase enzyme.

Immediately after infection there is a very high rate of viral turnover after which equilibrium is established (fig. 2.3). At this stage the infection may appear to be clinically latent, but up to 10,000 million new virions are produced each day. As chronic infection progresses, all cells possessing CD4 receptors (particularly the T helper lymphocytes) are depleted from the body in the absence of ARV drug intervention. However, with ARV drug intervention viral load is suppressed resulting in immune system rebound (fig. 2.4). The T helper cell is often considered to be the conductor of the immune system 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 recognized that some individuals rapidly develop severe immunosuppression whereas others may have been living with HIV for many years while maintaining a relatively intact immune system. It is likely that host and environment related factors contribute to this variation.

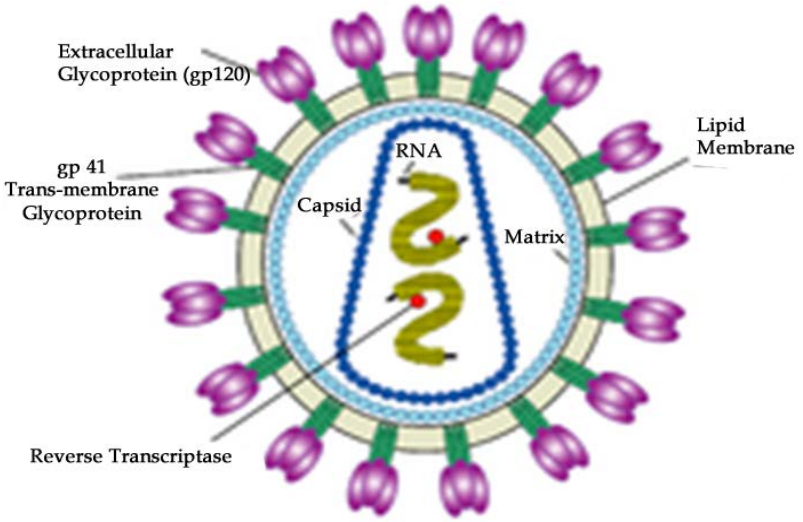

Figure 2.1: The structure of Human immunodeficiency virus (HIV). Two molecules of single stranded RNA are shown within the nucleus. The reverse transcriptase polymerase converts viral RNA into DNA

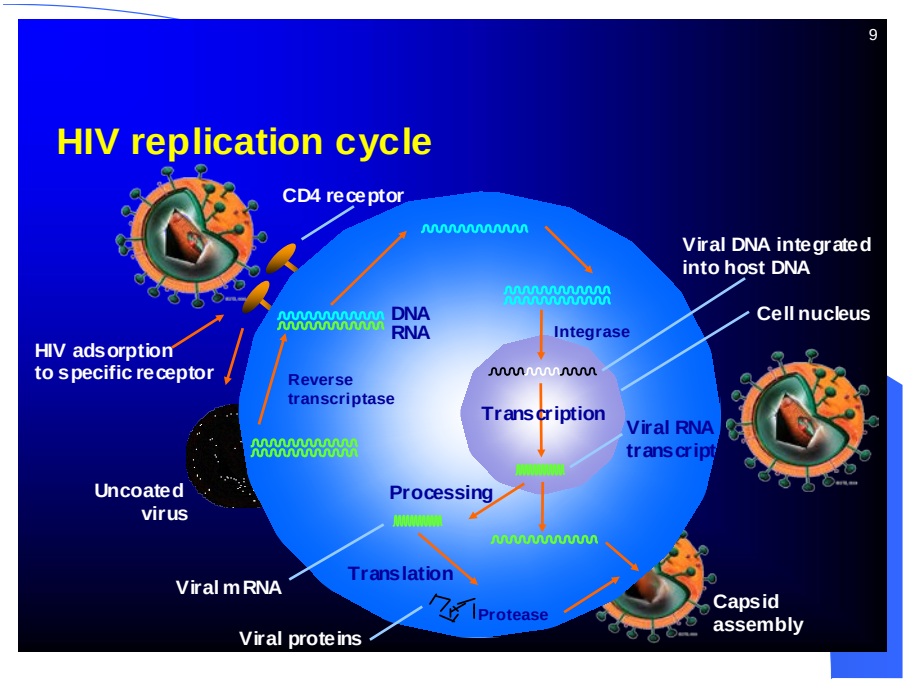

Figure 2.2: The process of attachment of HIV to host CD4 cell and various steps in the replication process

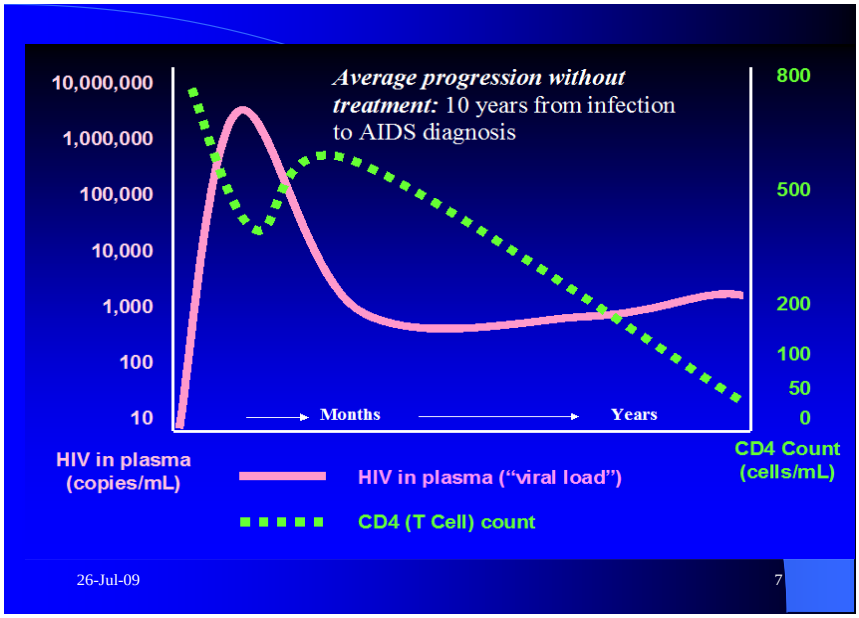

Figure 2.3: The relationship between CD4 count and viral load without antiretroviral drug intervention

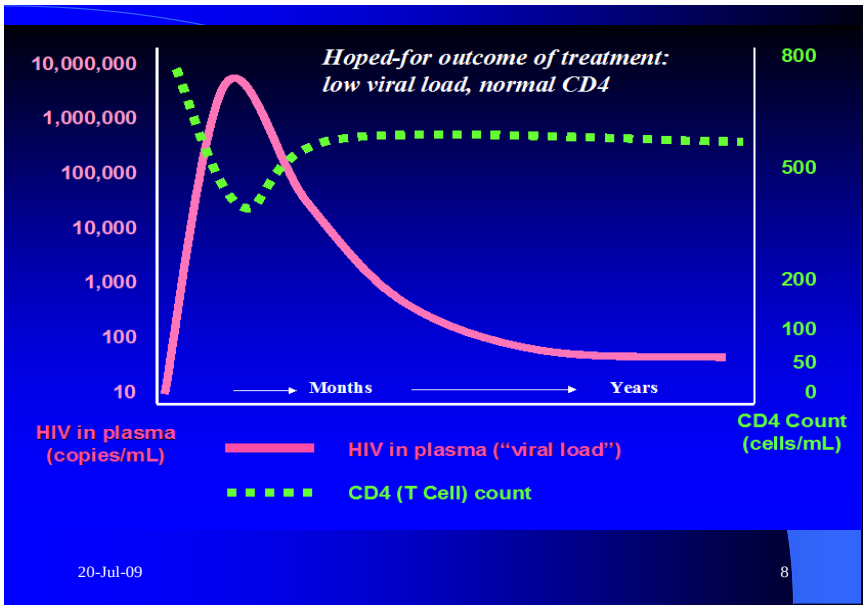

Figure 2.4: The relationship between CD4 count and viral load with antiretroviral drug intervention

2.2 CLINICAL MANIFESTATIONS OF HIV INFECTION

The consequences of untreated HIV infection can be classified broadly into four categories as follows according to Date and Fisher.

1. Opportunistic infections: these are infections that would not normally cause disease in immunocompetent hosts. Examples include *Pneumocystis carinii* pneumonia (PCP) and cytomegalovirus (CMV).
2. There are also infections that can occur in immunocompetent hosts but tend to occur more frequently and severely and mostly atypically in the context of underlying HIV infection.
3. Malignancies, particularly those that occur rarely in immunocompetent population. These include Kaposi's sarcoma (KS) and non Hodgkin's lymphoma.
4. Direct manifestation of HIV infection. These include HIV encephalopathy, myopathy, and enteropathy.

Additionally, almost 50% of HIV infected individuals develop a flu-like illness at seroconversion. This primary HIV infection is characterized by fever, arthralgia, pharingitis, rash and lymphadenopathy and in some cases oropharingeal candidiasis. Although the clinical course of HIV disease varies from person to person, there is a fairly consistent and predictable pattern that enables patients to be classified into one of three groups regarding their clinical status. These are asymptomatic, symptomatic or AIDS [9]

Asymptomatic/Clinical Latency

The majority of people with HIV infection are asymptomatic for a substantial but variable length of time. However the virus continues to replicate and the person is infectious. Some studies suggest a median time of 10 years from infection to development of AIDS, though some patients' progress much more rapidly others may remain symptom free for up to 15 years. Without testing most asymptomatic individuals may not be aware they are carriers of this deadly virus.

One of the factors associated with disease progression is old age. Some protective genetic factors are also recognized as playing an important role in the rate of disease progression Recent research findings have convincingly shown that some strains of HIV are associated with rapid progression from infection to disease. In some cases a period of about two years maximum is needed for an infected individual to develop AIDS. Gender and pregnancy per se do not appear to influence the rate of progression although women may fare less well for a variety of reasons [9].

A subgroup of asymptomatic individuals have persistent generalized lymphadenopathy (PGL) defined as lymphadenopathy (>1cm) at two or more extra-inguinal sites for more than three months in the absence of causes other than HIV. The nodes may disappear with disease progression.

Symptomatic HIV infection: As infection progresses, the viral load rises. The CD4 count falls and the patient develops a spectrum of signs and symptoms. The clinical

picture then becomes the direct result of HIV and associated immunosuppression. In an individual patient the clinical consequences of HIV related immune dysfunction depend on at least three factors.

a) The microbial exposure of the patient throughout life. Many clinical episodes represent reactivation of previously acquired infection which has been latent.
b) The pathogenicity of organisms encountered. High-grade pathogens such as Mycobacterium tuberculosis, candida, and the herpes viruses are clinically relevant even when immunosuppression is mild and will thus occur earlier in the course of the disease. Less virulent organisms occur at later stages of immunodeficiency.
c) The degree of immunosuppression of the host. When patients are severely immunocompromised (CD4 count < 100/mm3) disseminated infections with organisms of very low virulence such as *Mycobacterium avium-intracellulare* (MAI) and cryptosporidium are able to establish themselves. These infections are very resistant to treatment mainly because there is no functioning immune response to clear the organisms. This hierarchy of infection allows for appropriate intervention with prophylactic drugs.

2.3 GOALS OF ANTIRETROVIRAL THERAPY

The goals of offering antiretroviral therapy (ART) to patients are many and include the following:

Maximal and durable suppression of viral replication and viral load reduction: This results in restoration and preservation of immunologic function. Ultimately there is

reduction of HIV-related morbidity and mortality. This also leads to significant improvement and prolongation of life which is also qualitative.

Another goal of therapy is to prevent or reduce mother-to-child transmission of viral pathogens**.** As maternal viral burden reduces as a result of efficacy of antiretroviral medicines the possibility of in-utero transmission to the fetus is considerably reduced. There are three levels at which an HIV infected mother can transmit the virus to the child. These are in-utero, intra-partum (during labor) and through breast feeding. All these can be affected if viral load reduction is significant.

One of the consequences of maximal and durable suppression of viral replication is the prevention of mutation and emergence of resistant viral strains**.** It is believed that mutant viral strains come about as a result of the normal process of viral replication. This implies that the longer the viruses are allowed to survive in an individual without intervention, the greater their chances of mutation and therefore ability to cause drug resistance. In trying to achieve these goals there is the need to be mindful of some guiding principles governing antiretroviral therapy program.

There must be the selection of a regimen that is capable of achieving the suppression of viral replication [10] which is devoid of too many troublesome side effects that can interfere with adherence. Secondly there is the need for preservation of future treatment options such that in case there is treatment failure or intolerable side effects, a change in regimen is possible. For this reason there is the need for rational sequencing of therapy.

Thirdly, maximizing adherence to therapy should be the bedrock of a successful therapeutic outcome. This calls for the need to invest in time and efforts to ensure optimum adherence to therapy.

2.4 BENEFITS OF ANTIRETROVIRAL THERAPY

The benefits derived from ART are enormous. These include the fact that

1. There is increased acceptance and patronage of voluntary counselling and testing.
2. There is increased awareness of HIV as more and more people are counselled and educated.
3. As more and more people improve both clinically and symptomatically which then reflect on their socio-economic lives, health workers become motivated to render more service to clients and patients.
4. As immune system restoration occurs with attendant reduction in morbidity and mortality, less resource is expended on palliative care and treatment of opportunistic infections.
5. As ART converts HIV/AIDS into a chronic condition, more adult sufferers live longer, the numbers of orphans are reduced, more children get the chance to be educated and play significant roles in society during adulthood.
6. Directly related to the above point is that households and businesses are kept intact. The negative impact of HIV on the socio-economic life of people is reversed.[10]

2.5 THE CONCEPT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

Since the first antiretroviral medicine zidovudine was discovered and demonstrated to have some positive results on the lives of HIV/AIDS sufferers, the gains made regarding therapeutic potency of this drug and other members of the class which were later discovered continued to gain momentum. It was soon discovered that neither mono-therapy nor dual therapy was able to provide sustainable suppression of viral replication.

Date and Fisher have reported that most studies evaluating triple combination of antiretrovirals have been designed with so-called “surrogate marker” end points, measuring the effects on laboratory parameters such as CD4 and HIV viral loads. These trials according to them, are generally smaller and shorter in duration than clinical end point studies that alternatively measure the impact of HAART on patient survival and disease progression. The first large clinical end point trial that demonstrated the superiority of triple drug combination over dual therapy was ACTG 320 [10].

Following the results of this trial the standard of care has been, where treatment is indicated, to use a combination of at least three agents. This concept is what is referred to as Highly Active Antiretroviral Therapy [HAART]. Subsequently the reduction in mortality and morbidity associated with HAART use has been demonstrated in routine clinical practice as well as in trials [10]. Commenting on the impact of HAART on livelihood, Kumar and Clark report that in many developed countries, HIV related

morbidity and mortality has declined dramatically since the introduction of potent ART. Justifying this assertion, they continue that in the USA, the age adjusted death rate from AIDS fell 48% between 1996 and 1997 and death rate across Europe fell five fold between 1995 and 1998. European data also showed a fall in AIDS defining illness (ADI) from 30.7 per 100 patient years of observation to 2.5 per 100 patient years between 1994 and 1998 with patients on HAART having a lower rate of ADI's than patients not on HAART. Indeed several authors have recognized the significant impact HAART has played in the lives of persons living with HIV/AIDS. In one such admission attributed to Pallela and others, it is said that the introduction of highly active antiretroviral therapy HAART has led to a significant reduction in AIDS-related morbidity and mortality [11]. However, if antiretroviral therapy fails to control HIV replication, viruses will gradually emerge with mutations that confer resistance to the drugs being used in the regimen, and the longer uncontrolled replication persists in the presence of these drugs, the higher the level of resistance that will emerge.

2.6 ANTIRETROVIRAL TREATMENT FAILURE

Antiretroviral treatment failure and for that matter drug resistance is a major impediment to optimum treatment of HIV-1 infection and is a major public health concern [12] and the global agenda of offering antiretroviral therapy to persons living with HIV/AIDS. Various researchers have done volumes of work relating to the subject. One research finding attributed to Dr. Roy Gulick of New York Presbyterian Hospital indicates that as many as one quarter of HIV patients have drug resistance, limiting their treatment options and raising their risk of AIDS and death. Montessori and others

recognize that up to 25% patients discontinue their initial HAART due to treatment failure and toxic effects of noncompliance within the first 8 months of therapy [11].

Despite the significant progress made in HIVAIDS care since the advent of highly active antiretroviral therapy (HAART), therapies continue to fail in a large number of cases, generally because of resistance which is primarily driven by sub-optimal adherence [13]. Development of resistance to antiretroviral drugs (ARVs) is a major impediment to optimum treatment of HIV-1 infection. Treatment failure of antiretroviral experienced patients may be defined virologically, immunologically, or clinically. Virologic failure is the inability to achieve maximum suppression of HIV replication (undetectable viral load <50 copies/ml), or the achievement of maximal suppression followed by virological rebound. Immunological failure denotes the achievement of a very low or undetectable viral load, but the continued decline of CD4+ cell count. Clinical failure of antiretroviral therapy describes the situation in which an individual exhibits disease progression in terms of new, recurrent or progressing AIDS related opportunistic infections or HIV related symptoms such as weight loss, fatigue and sweats. Clinical failure can thus be used to monitor efficacy of antiretroviral therapy in resource constrained settings where CD4+ cell count or viral load testing is unavailable.

One troubling aspect of antiretroviral treatment failure is the fact that a significant number of patients begin treatment with transmitted drug resistant (TDR) strains of HIV referred to as primary resistance [12, 14]. Robert W. Shafer reports that there have been

many small studies of the prevalence of HIV 1-drug resistance in previously untreated persons in the United States and Europe. According to Shafer, a large study conducted in the United States involving about 2,035 patients revealed significant increase in prevalence of antiretroviral drug resistance among previously untreated persons with HIV-1. A summary of results indicates that the overall percentage of patients' samples with genotypic resistance to one or more drug classes increased from 5% and 10% in 2000 and 2001 to 14% and 16% in 2004 and 2005[15]

Additionally, resistance rates to non-nucleoside reverse transcriptase inhibitors (NNRTIs) increased from 2% to 10%. Resistance to zidovudine, a nucleoside reverse transcriptase inhibitor (NRTI) for example occurs with accumulation of mutations whilst single-point mutation will confer a high level of resistance to all three non-nucleoside (NNRTIs) reverse transcriptase inhibitors namely Nevirapine, Efavirenz and Delavirdine.

Other research findings have indicated that antiretroviral therapy is most effective the first time it is prescribed. Suppression of plasma HIV-I RNA replication to undetectable level is achieved up to 90% of the time when patients start their first triple-drug regimen [16]. The likelihood of achieving this degree of suppression however, decreases with each subsequent treatment regimen. Undetectable levels of HIV-I RNA are achieved in only one third or less of patients who have had previous exposure to two or three of the approved classes of ARV drugs that is NRTIs, NNRTIs and PIs (protease inhibitors).

Citing the causes of antiretroviral treatment failure some researchers mention important predictors of initial treatment regimen failure as advanced immunodeficiency (a diagnosis of AIDS or a CD4 cell count of less than 200/mm^3), a high plasma HIV-I RNA level and less than 95% adherence to therapy. Others include the narrow margin of efficacy of available ARVs, complex dosing schedules, side effects of the medicines, coexisting conditions that can compromise adherence, as well as large variations in the pharmacokinetics of the drugs. [17]

2.7 MECHANISM OF VIRAL REPLICATION AND HIV MUTATION

As HIV replicates, mutations in the HIV genome develop due to errors in the transcription of RNA to DNA by the viral enzyme reverse transcriptase [18]. When these errors are introduced into viral genes, a mutation may result. If the mutation occurs in one of the HIV proteins that is a target of an antiretroviral drug, the result may be decreased susceptibility or resistance to that drug, and lack of inhibition of viral replication by that drug. All progeny virions that are produced from a cell harboring mutant, resistant virus contain the same mutation or set of mutations. Approximately one mutation is introduced into the virus genome with each cycle of viral replication [18]. Because HIV replicates at such a high rate, roughly one to 10 billion viral particles are produced daily [19].Virtually all possible mutations in the HIV genome are generated within a patient on a daily basis. In this way, all HIV patients, including those naïve to therapy, harbor diverse population of viruses with differing susceptibilities to the currently available antiretroviral drugs. Because of the incidence of treatment failure,

there is now a strong advocacy for resistance testing where resources will permit even before treatment initiation.

2.8 RESISTANCE TESTING

Resistance testing is essentially a study of the genetic ability of the HIV virus to undergo mutations and also the patterns of mutations which render antiretroviral medicines inactive against the virus. Generally, there are two types of resistance testing that can be done. These are genotypic and phenotypic testing [20].

Genotypic resistance test reports the presence of specific mutations in the amino acid sequences of the HIV genome that encode the reverse transcriptase or protease enzymes, the targets of the HIV reverse transcriptase and protease inhibitors, or the part of the HIV genome that encode the reverse transcriptase or protease enzymes, the targets of the HIV reverse transcriptase and protease inhibitors, or the part of the HIV genome that encodes a specific region that is the target of the HIV entry inhibitor. Simply put, genotypic testing looks at the HIV present in a person's blood and examines it to see what mutations if any exist.

Phenotypic resistance testing on the other hand measures the concentration of drug needed to inhibit the replication of a patient's virus. Typically, this is quantitated by specifying the concentration of drug needed to inhibit 50% or 90% of virus replication (IC50 or IC90), or by comparing the fold-change in drug concentration required to inhibit the replication of the patient's virus compared to a representative, wild type,

sensitive virus isolate. In simple terms, this type of test takes virus and exposes it to different concentrations of HIV medications to determine which drugs are effective.

2.9 AVAILABLE ANTIRETROVIRAL DRUGS AND MECHANISMS OF ACTION

Research into the treatment of HIV infection has resulted in the development of five antiretroviral (ARV) drug classes [21]. Another system of classification looks at six classes of antiretroviral medicines. Coffey and Peiperl recognize chemokine coreceptor antagonists as one major class with two subclasses namely CCR5 antagonist and CXCR4 antagonist [22] while considering fusion inhibitors as a separate class of its own. The various classes and their members are listed below according to Stanic and Grana.

Nucleoside/Nucleotide Reverse Transcriptase inhibitors (NRTIs):

Abacavir, Didanosine, *Emtricitabine*, Lamivudine, Stavudine, Tenofovir and Zidovudine. These are phosphorylated intracellularly and then inhibit the viral reverse transcriptase enzyme by acting as false substrate.

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs):

Delavirdine, Efavirenz and Nevirapine. These inhibit the reverse transcriptase enzyme by binding to its active site. They do not require prior phosphorylation and can act on cell-free virions as well as infected cells.

Protease Inhibitors: *Amprenavir*, *Atazanavir*, *Fosamprenavir*, *Indinavir*, Lopinavir/ ritonavir Nelfinavir, *Ritonavir, Saquinavir and Tipranavir*.

These bind to the active site of the HIV-1 protease enzyme preventing the maturation of the newly produced virions so that they remain non infectious.

Entry Inhibitors: there are two subclasses, namely fusion inhibitors and chemokine coreceptor inhibitors. An example of fusion inhibitor is *Enfuvirtide* while *Maraviroc* belongs to the Chemokine Coreceptor inhibitor subclass. The target of action of these is the attachment/ entry stage in the HIV replication cycle. The linear 36-amino acid synthetic peptide inhibits fusion of the cellular viral membranes [23].

Integrase Inhibitor. an example is *raltegravir*

In Ghana, the antiretroviral medicines available belong to the first three classes mentioned above. Fusion inhibitors, Integrase inhibitors and Chemokine Coreceptor Antagonists are not available. Even among the first three classes that are available, not all the individual members are available. All drugs written in italics are not available. Therefore the limited availability of antiretroviral drugs places some limitations on the choice of medicines for individual patients. The problem becomes worse especially when patients fail on their first line regimen and have to be switched to second line.

2.10 RECOMMENDED ART REGIMEN

Different countries have slightly different treatment protocols regarding drug combinations for managing persons living with HIV/AIDS (PLWHAs). However these protocols must fit into the general framework or recommendations of the World Health Organization. In Ghana, the recommended regimen below is for the treatment of ART-naïve persons. This is based on evidence from other ART programmes worldwide and recent local experience. These recommendations are also based on the effectiveness of the drug, pill burden, dosing in relation to food, toxicity, dosing frequency, nutritional

requirements, convenience and drug interaction profiles, resistance to ARV, availability and cost. Globally, all antiretroviral therapy programmes subscribe to a system known as highly active antiretroviral therapy (HAART). This means that every patient is given a minimum of three ARVs from different classes for maximum and durable suppression of HIV replication. For this and other reasons cited earlier the following triple regimens are accepted in Ghana.

- Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and 1 Non-nucleoside Reverse

  Transcriptase Inhibitor (NNRTIs)
- 2NRTIs and 1 Protease inhibitor (PI)
- 2NRTIs and 2 PIs. The 2 PIs in this particular combination are considered as one ARV, because the second PI, usually ritonavir, is in low dose and is used to boost the blood level of the first PI.

In addition to the general principles, specific drug combinations are also recommended below and described as either first line or second line drugs. Within the first and second line categories, there are first and second options.

Example of specific first line regimen

[Zidovudine + Lamivudine] + Nevirapine or alternatively [Stavudine+Lamivudine] + Nevirapine

[Zidovudine + Lamivudine] + Efavirenz or alternatively, [Stavudine +

Lamivudine] + Efavirenz

Example of specific second line regimen

[Abacavir, Tenofovir] + Nelfinavir or alternatively, [Abacavir, Tenofovir] + Lopinavir/r [Didanosine + Abacavir] + Nelfinavir or alternatively, [Didanosine + Abacavir] + Lopinavir/r.

2.11 SIDE EFFECTS OF ANTIRETROVIRAL DRUGS

In spite of the huge success of antiretroviral medicines, adverse effects of these drugs ranging from mild ones to very serious ones sometimes poses enormous challenges on patients and health workers alike. According to Montessori et al, antiretroviral therapy can have a wide range of adverse effects on the human body. Common but mild effects occurring early in most antiretroviral regimens include gastrointestinal effects such as bloating and nausea. These may be transient or may persist throughout therapy

Other common effects include fatigue and headache caused by zidovudine and efavirenz induced nightmares. More serious ones include anemia due to zidovudine, stavudine induced peripheral neuropathy, hypersensitivity reactions associated with abacavir and nevirapine. Lactic acidosis, hepatotoxicity, lipodystrophy, abnormal glucose metabolism and heart related adverse effects. These and others that have not been enumerated sometimes make therapy difficult for patients and negate some of the positive outcomes of ART.

2.12 ADHERENCE TO ANTIRETROVIRAL THERAPY

Although there is no universally accepted definition, medication adherence may be defined as the extent to which a patient takes a medication in the way intended by a

health care provider. The terms adherence and non adherence are meant to be nonjudgmental, statements of fact rather than expressions of blame toward the patient or provider. Non adherence to medication, in general, is very common. Typical adherence rates for medications prescribed over long periods of time are approximately 50-75% [24, 25]. It is well established that very high adherence is needed to ensure the success of antiretroviral therapy. Notably, recent research has identified the highest risk of developing drug resistance with relatively high (80-<90%) adherence. Other research findings indicate that at least 95% (near perfect) adherence to therapy is required in ART for meaningful outcomes. [26]

Though adherence is not the only determinant of ART failure or success it has been found to be a significant factor. Other factors include genetic differences in drug metabolism, severe baseline immune suppression, prior drug resistance, and concurrent opportunistic infections. Adherence to ART, however, is one of few potentially alterable factors determining outcomes for patients with HIV. Nonetheless, it is well known that health care providers, in general, are unskilled at assessing and improving medication adherence.[27,28,29] The final crucial step toward ameliorating the impact of HIV the actual taking of the medications is often neglected. Periodic assessment of adherence to therapy or otherwise is essential in helping patients adhere to therapy. Methods of assessment include pill count, pharmacy refill records, medication event monitoring systems (MEMS) and biological markers such as CD4, and viral load estimations. [30]

CHAPTER THREE

METHODS

3.1 ORGANIZATION OF THE STUDY

The study which was essentially retrospective was organized in two phases. The first phase was designed to examine patients' folders and to collect data relevant to the topic under study. The second phase involved personal interviews of patients who satisfied the requirements of participating in the study. For the purpose of the first phase a data collection tool (appendix 1) was designed and used.

3.2 SAMPLE SIZE

Altogether, one hundred and sixty four (164) patients were investigated as opposed to one hundred and eighty originally envisaged. The number fell slightly short of expectation because some patients' folders could not be retrieved.

3.3 INCLUSION CRITERIA

The criterion for selection of study participants was based on the fact that patients had taken or were taking second line regimen. Before the study was initiated, a database of all HIV/AIDS patients who had been prescribed second line regimen at one time or the other at Komfo Anokye Teaching Hospital within the study period of February 2004 and April 2009 was generated from pharmacy records. The key indicator for selecting this category of patients was that their regimen contained drugs such as Nelfinavir or Lopinavir/ritonavir which are protease inhibitors and Abacavir, Didanosine and

Tenofovir which are nucleoside reverse transcriptase inhibitors but are not used routinely. No restriction was employed regarding how long participants had been on treatment.

3.4 EXCLUSION CRITERIA

The following categories of patients were excluded from the study.

1. Patients whose regimen at the time of study did not contain any of the second line drugs mentioned above and were considered to be psychologically stable to respond to issues in the questionnaire.
2. Pediatric patients aged less than eighteen years. This is due to the perceived difficulty of responding to the issues in the questionnaire adequately.
3. Patients whose folders could not be available to be examined
4. Those who for personal reasons declined to participate in the study.
5. Those whose folders were found but did not contain enough information as required.

3.5 LIMITATION

One major limitation of the study was the inability to perform resistance testing on the participants. This is largely due to the fact that facility for testing was not available. For this reason no blood sample, body fluid or human tissue was used in the study.

3.6 DATA COLLECTION

As has been indicated, data collection was organized in two phases as described below.

3.6.1 Phase 1

Two sets of data were collected under phase 1. These are clinical data and demographic data such as age, gender, educational background, marital, social and employment status. These were necessary because one of the objectives of the study is to be able to provide or describe the demographic characteristics of the participants. Secondly it is also important to see if there exists any correlation between treatment failure and demographic data.

The clinical data collected as well as their relevance to the study are listed below.

- ***Date of antiretroviral therapy (ART) initiation.***

  One of the strong points of the ART programme is structured monitoring of therapeutic progress. For this reason it is important to know when treatment is initiated and the baseline parameters taken so that subsequent data are compared for proper judgment and the necessary interventions made.

- ***CD4 at treatment initiation (baseline CD4).***

  CD4, viral load assays and clinical manifestations of disease conditions are very vital in the monitoring process. The CD4 values obtained are used to determine how patients respond to treatment immunologically.

- ***The highest CD4 recorded before decline (Peak CD4)***

  The peak CD4 value is relevant in determining the point at which immunological response began to show a downward trend.

- ***ART initiation or continuation regimen.***

  It is a fact that ARVs are effective the first time they are prescribed. For this reason any attempt to initiate to continue ARVs especially in treatment experienced patients must ensure maximization of results. Examining the treatment initiation/continuation regimen was important in assessing the appropriateness or otherwise of the participant's medication.

- ***Date of change or switch to second line regimen.***

  One of the goals of ART is to have therapeutic option in case treatment failure develops while the patient is on a particular regimen. Long delay on ineffective regimen becomes a waste of resources and needless suffering to the patient. It also has the potential to compromise treatment outcome due to development of more resistant strains. The date of change was therefore used to determine whether patients were offered their treatment options at appropriate time or not.

- ***Record of adherence or non adherence to therapy.***

  From the folders, results of periodic pill count of medication left over which though cannot be accurate predictor of adherence but reliable in some cases was taken. This was added to the results of adherence assessment obtained in phase two of the study.

- ***Reasons for change.***

  In as much as change of regimen is necessary at some point in a patient's treatment, it is also a fact that too frequent changes of regimen soon leaves the patient with no therapeutic option at the time it is most needed. It was therefore

important to assess whether there were enough justifications for change or otherwise.

From the information collected, two data items were estimated. These are:

1. The duration in months for which each patient was on first line. This was estimated as the time interval between the date when treatment was initiated and the time when it was changed to second line.
2. The peak time in months. This was estimated at the time interval between when treatment was begun and the time when the highest CD4 value was measured.

3.6.2 Phase 2

The second phase involved interviewing study participants. For this purpose a questionnaire (appendix 3) was developed and administered to respondents. Patients were posed the various questions and their responses recorded. Before soliciting their participation, a statement of consent (appendix 2) designed for that purpose was introduced to the patients and discussed thoroughly.

Issues discussed on the consent form include the following:

- Introduction of the interviewer and the purpose of the study,
- Respect of the patient's right to either participate or not,
- Risk or benefit of participating in the study and
- Assurance of confidentiality, avoidance of stigma and discrimination.

After participants had satisfied themselves with the content of the statement of consent, they were requested to either append their signature or thumbprint a portion on the form to indicate that they agreed to participate in the study. The questionnaire was used to collect the following information from participants:

- ***History of infection/disease***

  History taking was necessary to gain understanding of the patient's lifestyle and the possible context in which infection is perceived to have taken place.

- ***Initial treatments and places/facilities where treatment was accessed.***

  Even before antiretroviral medicines are offered, countless patients receive various treatments like herbal products of unknown chemical composition that have the potential to jeopardize future antiretroviral therapy. Such knowledge is vital for initial decision making and subsequent monitoring of treatment outcome.

- ***History of previous exposure to antiretroviral/other medicines.***

  Previous exposure to antiretroviral medicines is one of the key determinants of treatment success. It was therefore important to find out whether or not exposure had occurred. This is also useful in constructing appropriate treatment initiation or continuation regimen.

- ***Types and combination of antiretroviral medicines used where applicable.***

  This is again necessary in constructing initiation or continuation regimen. If a patient had not been doing well for instance on a particular combination it will not be clinically prudent to continue treatment on that same combination.

- ***Supply of antiretroviral medicines, regularity, cost and monitoring systems.***

  These indicators are also crucial in assessing the drug supply situation which, to a large extent has tremendous impact on treatment adherence and success.

- ***Records of adherence to therapy and factors that militated against adherence.***

  With patients who had received previous exposure to ARVs it was important to assess their record of adherence in order to know whether there was any relationship between non adherence and treatment failure and also to offer appropriate counseling. Problems that brought about previous non adherence are then addressed during the counseling sessions. In assessing the level of non adherence among patients, three parameters were used. These are patient's self report, pharmacy drug refill records and information from folders. Participants were asked whether they had interrupted treatment before, how many times this had happened and the duration of interruption.

Phases one and two adherence records were pooled together. All patients whose records indicated that they had interrupted treatment before for periods ranging from two weeks to eight weeks and more with frequency of interruption being twice or more, were described as poor adherents to treatment. All other patients whose records did not show treatment interruption were said to have good adherence to treatment.

At the end of the data collection process all the information from the data collection tool and questionnaire were aggregated and put on another tool designed for that

purpose described as data summary sheet (appendix 4). The aggregated data which constituted the entire results of the study were then analyzed using computer software called Statistical Package for the Social Sciences (SPSS) and other statistical tools. The results are presented in chapter 4 of this thesis.

CHAPTER FOUR

RESULTS

4.1 DEMOGRAPHIC CHARACTERISTICS

Out of the total number of 164 patients, 110 (67%) were females and 54(33%) males giving a male to female ratio of approximately 1:2. With respect to age, 17.7% (29) patients belonged to the age group 21-30years, 36.6% (60) patients aged 31-40 years, and 29.9% (49) patients were 41-50 years. Altogether, 84.1% 0f the patients were within the age bracket of 21-50 years (Fig. 4.1)

On employment status, 8% were government employees, 41(25%) were unemployed and 93(57%) were either self employed or worked for others (Fig.4.2). Twenty eight patients (17.1%) were rural dwellers while 134(81.7%) were urban dwellers (Fig. 4.3). Regarding marital status 75 (46%) of the patients were married and 89(54%) were single (Table 4.1). The results indicate that 132 (80.5%) had either no formal educational background, 24(14.6%) had secondary level of education with only 8 (4.9%) having tertiary level of education (Table 4.2).

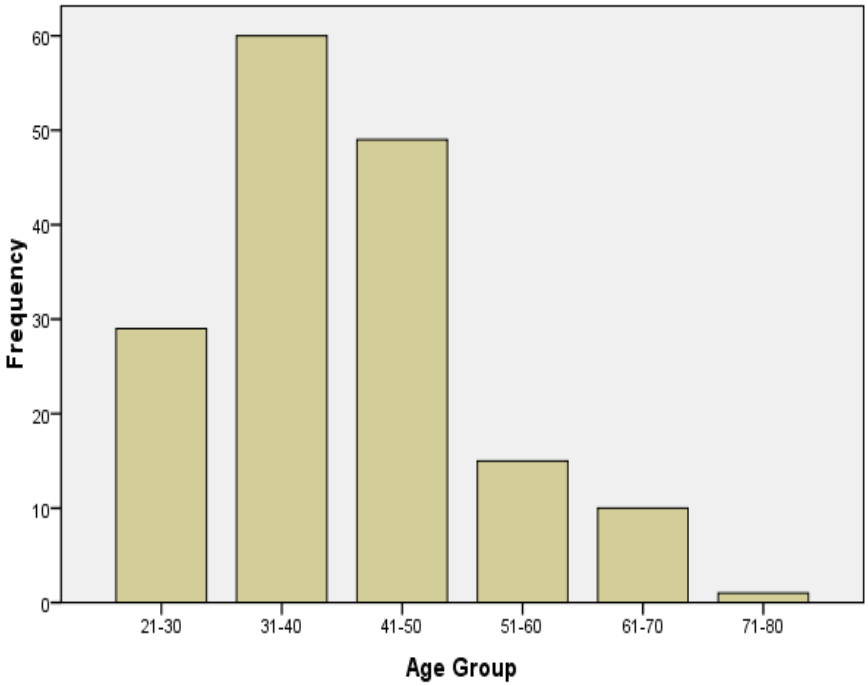

Figure 4.1: Age Distribution

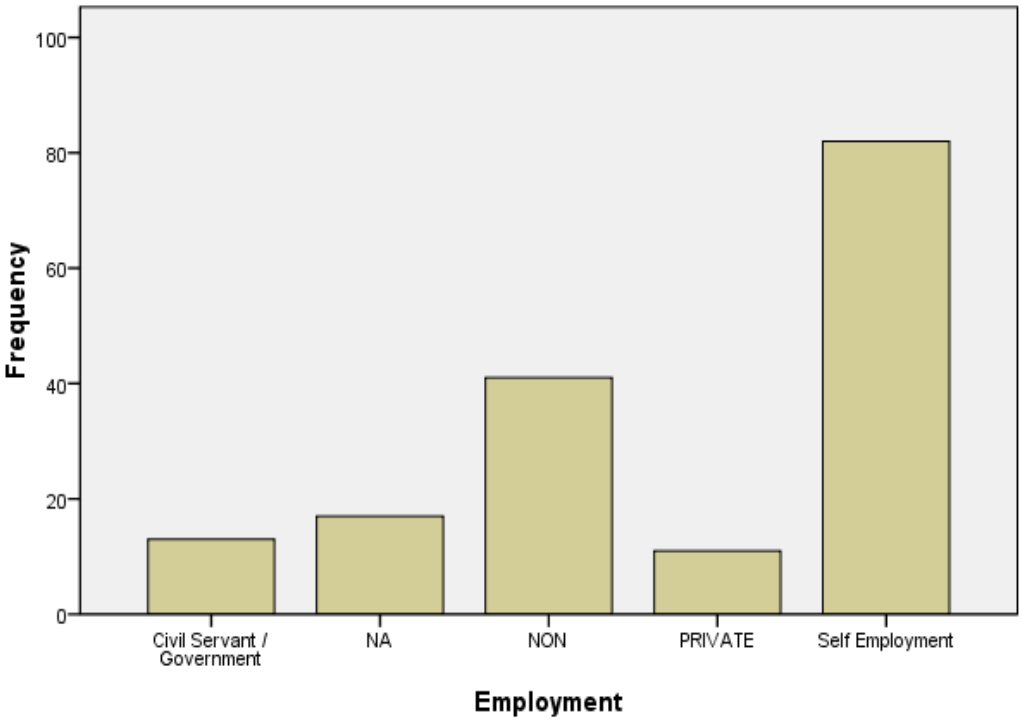

Figure 4.2: Distribution of Employment Status

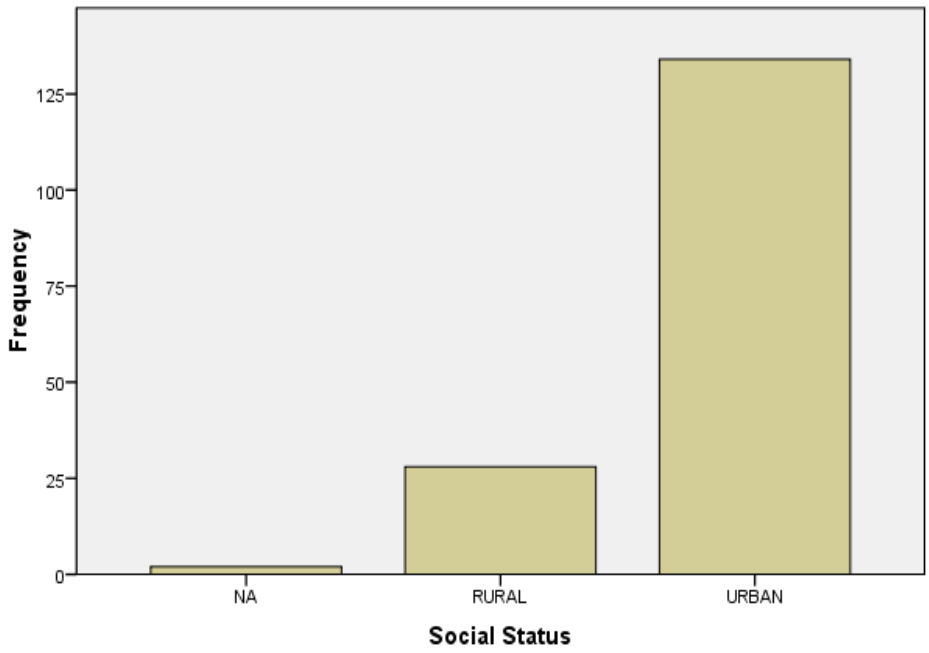

Figure 4.3: Distribution According to Social Status

Table 4.1: Marital Status

	Frequency	Percent	Valid Percent	Cumulative Percent
CO-HABITATION	3	1.8	1.8	1.8
DIVORCED/SEPARATED	35	21.3	21.3	23.1
MARRIED	75	45.7	45.7	68.9
SINGLE	23	14.0	14.0	82.9
WIDOWED	28	17.1	17.1	100.0
TOTAL	164	100.0	100.0	

Table 4.2: Educational Background

	Frequency	Percent	Cumulative Percent
None	38	23.2	23.2
Primary	94	57.3	80.2
Secondary	24	14.6	95.1
Tertiary	8	4.9	100
Total	164	100	

4.2 OVERVIEW OF ART: DIAGNOSIS AND MANAGEMENT

The results demonstrated the presence of HIV 1 as the predominant type constituting some 77% (Fig. 4.4). The four main first line regimen types were AZT.3TC.EFV (28%), AZT.3TC.NVP (22.6%), D4T.3TC.EFV (16.5%) and D4T.3TC.NVP (18.9%) making up 86% (Table 4.3). The stavudine (D4T) group showed better response than the zidovudine (AZT) group. Between the two D4T groups those on EFV showed a higher peak than NVP group (Fig. 4.5). However, in terms of the actual quantum of change there may not be any significant difference. Of all the various regimen types the one containing didanosine, abacavir and ritonavir boosted lopinavir produced the highest response (Fig 4.6). Twenty two (13.9 %) of the patients who were infected with either type 2 or 1&2 HIV were found to be taking regimen containing non nucleoside reverse transcriptase inhibitors such as nevirapine or efavirenz which are known to be inactive against type 2 HIV.

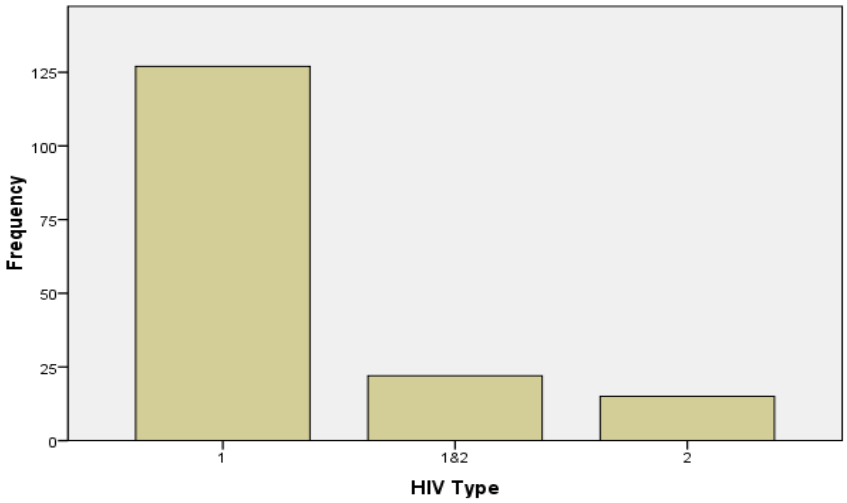

Figure 4.4: Distribution of HIV Type

Table 4.3: Regimen type Distribution

Regimen Type	Frequency	Percent	Valid Percent	Cumulative percent
3TCTDFLPVr	1	.6	.6	.6
AZT3TCEFV	46	28.0	28.0	28.7
AZT3TCLPVr	4	2.4	2.4	31.1
AZT3TCNFV	9	5.5	5.5	36.6
AZT3TCNVP	37	22.6	22.6	59.1
AZTTDFLPVr	1	.6	.6	59.8
D4T3TCEFZ	27	16.5	16.5	76.2
D4T3TCLPVr	3	1.8	1.8	78.0
D4T3TCNFV	3	1.8	1.8	79.9
D4T3TCNVP	31	18.9	18.9	98.8
DDIABCLPVr	2	1.2	1.2	100.0
Total	164	100.0	100.0	

Table 4.4: Peak Time Vrs. Treatment failure

Month	Frequency	Percent	Cumulative Percent
00-10	83	50.6	50.6
11-20	57	34.8	85.4
21-30	15	9.1	94.1
31-40	7	4.3	98.8
51-60	2	1.2	100.0
Total	164	100.0	

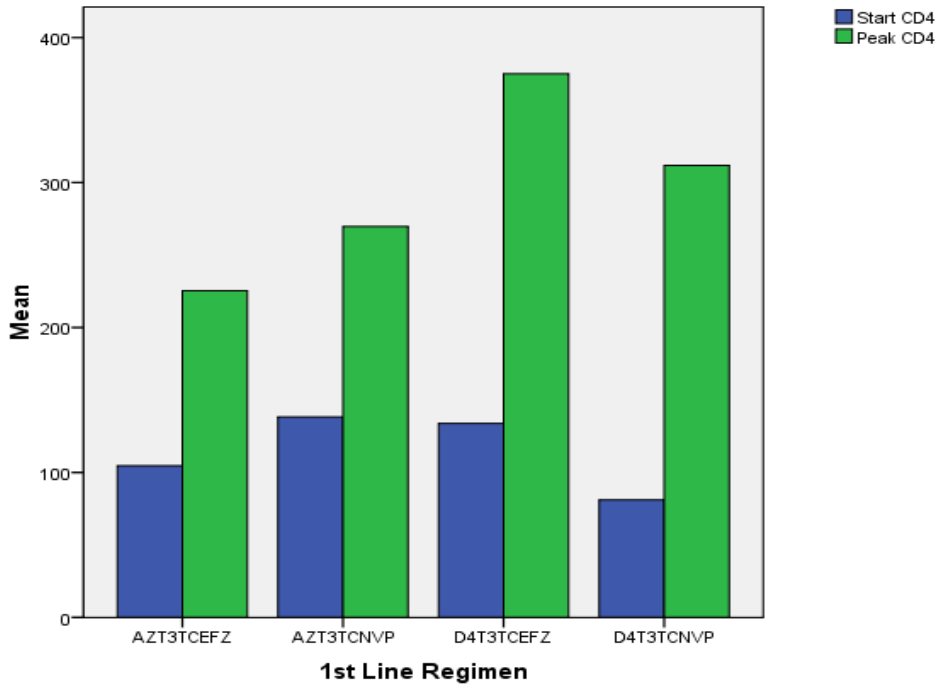

Figure 4.5: Initial and peak CD4 against the 4 main 1st line regimen

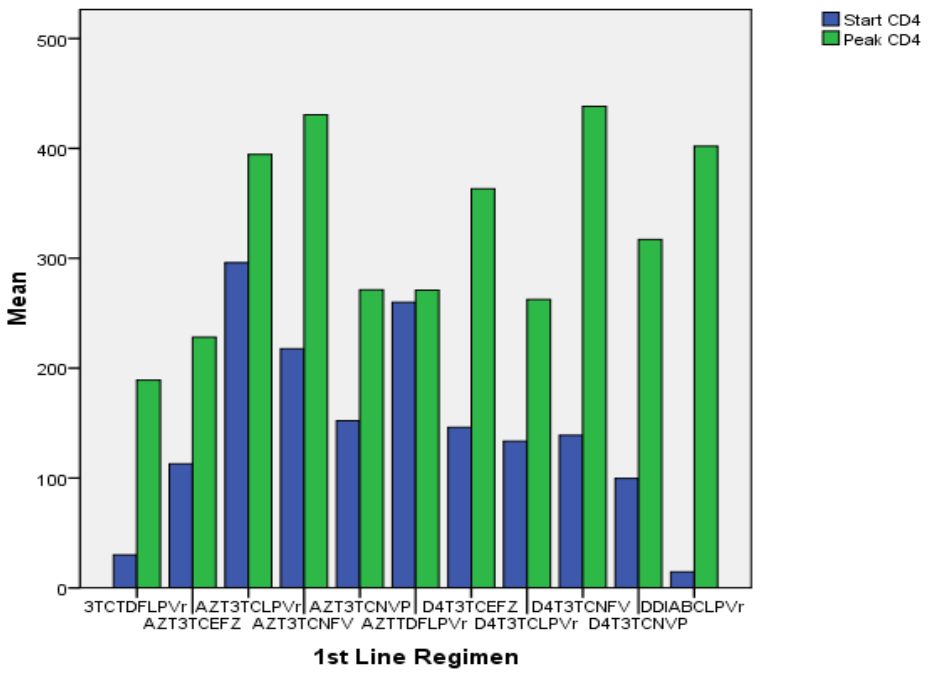

Figure 4.6: Initial & Peak CD4 trends against drug combination types

4.3 PREVALENCE OF TREATMENT FAILURE

With exception of six(6) patients of the study population of 164 who were on protease inhibitor based regimen as a result of side effects experienced on non nucleoside reverse transcriptase inhibitor based regimen, the rest 158 (96%) had actually developed treatment failure on treatment initiation or continuation regimen. The prevalence was calculated by dividing 158 by the total number of patients on treatment 4,323 and multiplying the result by 100%. This gave a figure of approximately 3.7%. The prevalence of antiretroviral treatment failure among adult population receiving therapy at KATH for the five years and two months period was therefore estimated to be 3.7%.

4.4 PEAK TIME OF TREATMENT FAILURE.

It was observed that by the 20th and 30th months after initiation of therapy, 85.5% and 94.1% of the study population respectively had reached the climax of their treatment on initiation regimen. Twenty three (14%) of the 164 patients never demonstrated any improvement in immunological response on their initiation therapy. Eighty three (50.6%) of the study population achieved maximum immunological response between zero and ten (0-10) months (Table 4.4).

4.5 CAUSES OF ANTIRETROVIRAL TREATMENT FAILURE

Forty percent (40%) of the study population admitted that their adherence to therapy had been poor, 60% of them claimed that their adherence to therapy had been good. On tuberculosis infection record, 14% (23 patients) had been infected with tuberculosis on one occasion or the other since they were diagnosed HIV positive. It was also observed that a significant number of participants had serious financial difficulties regarding the payment of five Ghana Cedis monthly and also for transportation to and from the hospital.

On previous exposure to antiretroviral medicines, It was found that 34(20.7%) of the study participants had been exposed to diverse combinations of anti-HIV medications before continuing treatment at KATH. This means that 79.3% of the study population was treatment naïve. Logistical constraints in terms of laboratory reagents and equipments like viral load machines as well as drugs were found to be challenges.

CHAPTER FIVE:

DISCUSSION

5.1 DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

Out of the total number of 164 patients, 110 (67%) were females and 54(33%) males giving a female to male ratio of approximately 2:1. This ratio compares very well with the statistics of the general HIV/AIDS population registered at KATH including those on therapy. One research finding indicate that female to male HIV infection prevalence ratios in some southern African countries ranged from 1.2:1 to 1.6:1, female to male ratios on HAART ranged from 0.8: 1 to 2.3: 1. The majority of the reports had female: male ratio on treatment exceeding 1.6.

Overall, there were more females on HAART than there were males and this was not solely explained by the higher HIV prevalence among females compared to males. The conclusion was that in most Southern African countries, proportionally more females are on HIV antiretroviral treatment than men [31]. Gender related treatment failure results could not obtained but are likely to follow the same trend. For instance the HIV/AIDS figures in Table 1.1 shows that many Sub Saharan African countries have more women with HIV than men. It is likely that socio-cultural and anatomical factors among others contribute to this unfortunate trend.

It was found that 18% (29) patients belonged to the age group 21-30years, 36% (60) patients aged 31-40 years, 30% (49) patients were 41-50 years. Altogether, 84% (138)

0f the patients were within the age bracket of 21-50 years. The 2008 HIV Sentinel Survey Report for Ghana has disclosed that HIV prevalence declined in all age groups except 40-45 and 45-49 year groups. Again resistance values and age distribution figures elsewhere could not be obtained for comparison. From this it can be seen that if the HIV/AIDS pandemic is allowed to go on unchecked the productive sector of our economy will be devastated.

Thirteen patients (8%) of the study population were found to be government employees, 17(10%) had their employment status not recorded, 41(25%) were unemployed and 93(56.7%) were either self employed or worked for others. The situation is likely to be a good reflection of the general HIV/AIDS population at KATH. These figures were taken at the time of treatment initiation when patient's clinical conditions were not too good. It may be necessary for another study to be carried out to look at the impact of ART on employment status or economic activity of persons living with HIV/AIDS.

Twenty eight patients representing 17% were rural dwellers while 134(83%) were urban dwellers. The wide disparity between urban and rural dwellers should be a matter of serious concern to all stake holders involved in our health care delivery system. It is a well known fact that most rural dwellers actually depend on traditional medicine rather than seeking intervention through orthodox medicine. It has been reported by Elujoba and others that Traditional African Medicine serves over 80% of Africa's population.

For this reason rural dwellers with HIV may not submit themselves to testing in order to be diagnosed [32]

The results show that 75(46%) of the patients were married, 89(54%) were single, widowed, divorced/separated or were co-habiting without formal marriage. It is not known how many of the study population acquired HIV through sexual relationship. One thing that is certain is that some 85% of study participants have sexual partners who may be sero-concordant with possible mutant strains of HIV. This is premised on the fact that sexual transmission accounts for some 85% of all HIV cases.

The results have also revealed that 132(80.5%) had either no formal educational background or had at best primary education. 24 patients corresponding to 14.6% had secondary level of education with only 8(4.9%) having tertiary level of education. It may be necessary to further investigate the relationship between HIV infection and educational background among the general HIV/AIDS general population. If the results confirm that infection prevalence rates are higher in poorly educated populations it will serve a useful purpose to intensify infection prevention activities among such population.

5.2 PREVALENCE OF TREATMENT FAILURE

The total number put on ART at Komfo Anokye Teaching Hospital as at April 2009 stands at 4,232 over a period of five years and two months. 158 out of the total of 164 study participants had actually experienced treatment failure on initiation/continuation therapy. This gives a prevalence rate of 3.73% as the percentage of patients who have

actually developed treatment failure over the five year period. It is important to state that the most significant indicator of treatment failure utilized in the study was immunologic failure using CD4 values.

As has been mentioned earlier, treatment failure among persons living with HIV/AIDS can be described in three principal ways. The other two are virological and clinical. As part of the clinical practice it is required that patients are monitored regularly to ensure effectiveness of treatment. Monitoring patients' immunological response to treatment requires regular laboratory assessment of CD4 values. By WHO definition patients are deemed to have failed treatment when there is a decrease in CD4 count to or below the baseline before treatment, or a 50% decrease from the on-treatment peak value (if known), or CD4 concentrations persistently less than 100 cells/µl [33], provided other causes like non adherence to therapy have been ruled out. In most cases clinical involvement was absent and patients looked very well symptomatically.

In very few cases viral load results were available to indicate that there was strong virological involvement. Not too many viral load results were available because patients could not afford the high cost of this vital laboratory service which in some cases was up to GHc100 or one million Cedis in the old currency. The prevalence rate of 4% seems to be a remarkable achievement if one compares this figure with what pertains elsewhere. For example a publication reported to have been sourced from New York Presbyterian Hospital states that "as many as a quarter of HIV patients have drug resistance."[34]

5.3 PEAK TIME OF TREATMENT FAILURE

It was observed that by the 20th and 30th months 85.4% and 94.1% respectively had reached the climax of their treatment on initiation regimen. Fourteen percent (14%) of the 164 patients never demonstrated any improvement in immunological response on their initiation therapy. What is more serious is that 83(50.6%) of the study participants achieved maximum immunological response between zero and ten (0-10) months.

The implication of this is that by the end of the 10^{th} month on treatment, more than 50% of patients on ART who are likely to fail treatment on initiation regimen would have actually failed. It is therefore necessary for clinical staff that enough details and history are taken during pretreatment interactions with patients so that effective monitoring programs are proactively drawn for such individuals before treatment initiation.

With the 14% of participants that never demonstrated any significant immunological response, it is likely that they initiated treatment with what is called primary resistance. This implies that the viruses in such individuals were non responsive to the drug combinations offered as initiation therapy. They are likely to have been infected with what is known as transmitted drug resistant (TDR) strains of viruses. Susan J. Little and other researchers have reported that among persons in North America, who are newly infected with HIV, the prevalence of transmitted resistance to antiretroviral drugs has been estimated at 1 to 11 percent. Hammer and colleagues also quoted 5% from Zambia [35] while Reuter and colleagues reported on figures from Germany by indicating that the overall prevalence of viral samples containing resistance associated mutations in new

infections was 9.9% [36]. Parenti and colleagues also presented values from Argentina where a figure of approximately 13% was quoted. It is essential to note that in addition to extrinsic factors associated with drug resistance, viral intrinsic factors also play significant roles in drug resistance.

5.4 CAUSES OF ANTIRETROVIRAL TREATMENT FAILURE

5.4.1 Logistical constraints

From the above made observations, it is clearly seen that logistical constraints can have a serious negative impact on treatment outcome. From the study it has emerged that (23) 14.1% of patients never demonstrated any improvement in immunological response on their initiation regimen. Out of this number only five were treatment experienced while 18 were treatment naïve. This implies that this group of treatment naïve patients began ART with resistant viral strains. If facilities for resistance testing were available, such patients could have been tested before initiating therapy thereby averting the situation of being initiated on ineffective regimen. The same reason accounts for why 22 patients (13.5%) who had either HIV type 2 or type 1&2 dual infection were put on non nucleoside reverse transcriptase inhibitor (nevirapine and efavirenz) based regimen which are known to be inactive against type 2 human immunodeficiency virus.

In trying to find out whether patients missed their appointments with clinicians or not, one prominent reason given by respondents was that they could not do laboratory investigations due to unavailability of laboratory reagents, including those for CD4

assessment. For this reason scheduled monitoring of immunological response was not always possible for clinicians to decide when it was necessary to intervene.

5.4.2 Drug Supply System

Another crucial issue relating to logistics is the drug supply situation. At one point or the other in the history of the ART programme, drug shortages have been experienced to the extent that simple first line drugs were affected. In some instances patients were issued with drugs for periods ranging between five days and two weeks. It is difficult at this point to say emphatically whether resistance developed in some patients as a result of this situation. However it is known that some patients who traveled long distances to access care at the clinic could not cope with the financial stress of visiting the clinic at very short intervals for their drug refills and therefore had very poor adherence which probably could have resulted in resistance development.

5.4.3 Previous Exposure to Antiretroviral Medicines

Another important factor responsible for antiretroviral treatment failure that the results seem to suggest is that of previous exposure of patients to antiretroviral medicines. The results indicate that 25 out of 34 (73.6%) patients who had been previously exposed had failed on initiation regimen before joining the program at KATH. Detailed statistical data regarding the causes of failure among this category of patients is not available.

However, responses gathered through the interviews reveal that some patients took ARVs received from various sources without any form of monitoring or pretreatment

adherence counseling. For this reason, pertinent issues like lifelong treatment, strict adherence to doses and frequency, side effects of drugs and other issues like interactions were not understood by patients. Even though the study has not been able to establish a strong association between previous exposure and treatment failure, it will be important that this subject is given further attention.

5.4.4 Poor adherence to therapy and financial difficulties

Treatment experienced patients who were fortunate to access treatment from private medical facilities with monitoring could not sustain treatment for long periods due to lack of financial resources to pay for antiretroviral medicines at very high cost, which in some cases run to two million Cedis monthly in the old currency or two hundred Ghana Cedis. Currently even though treatment is subsidized by government and patients are expected to pay GH¢ 5.00 per month for a comprehensive package of healthcare, more than 50% of patients who attend clinic at KATH report of inability to pay. Due to the weak financial strength on the part of some patients their record of regular drug refill is unimpressive thereby affecting adherence.

The study has not been able to prove convincingly that there is a strong relationship between treatment failure and educational background and for that matter occupational or employment status. However one fact that has been strongly established through the study is that lack of financial resources is a major setback to antiretroviral drug adherence. Adherence to therapy is considered to be one of the key determinants of treatment success. Research has proved that at least at least 95% adherence is required

for any meaningful treatment success to happen. From the results it is clear that 66(40%) of respondents admitted that their adherence has been poor. It is very likely that this figure could be more because two of the methods of assessing adherence relied heavily on the patients' inputs such as pill count and patient self report.

5.4.5 Co-morbid Conditions

On record of tuberculosis infection it was realized that 23 patients (14%) had been treated for tuberculosis on one occasion or the other. If tuberculosis comes as a co-morbid condition, adherence to therapy becomes extremely difficult because pill burden becomes unbearably high. HIV/AIDS patients on therapy are given a minimum of three drugs. Treatment of TB, especially during the intensive phase (first two months of treatment) requires four drugs. The patient may be taking two tablets of co-trimoxazole daily for prophylaxis against opportunistic infections. In such a scenario drug-drug interactions, increased side effects profile and pill burden can complicate therapy and seriously compromise treatment outcome. Since HIV/AIDS patients are not insulated from the effects of other ailments, they are vulnerable to other disease conditions from asthma to hypertension, diabetes, cancers and many more. Taking HIV drugs for life in a situation of co-morbid conditions can to some extent erode the gains expected from taking ART.

5.4.6 ART Initiation Regimen

As has been mentioned in the methods, treatment initiation regimen is very crucial in achieving sustainable suppression of viral replication. Results from the study cannot tell

specifically which regimen type caused the greatest or the least resistance. The results only indicate that there were more patients on some regimen types than others as can be seen below. Those on Zidovudine, lamivudine and efavirenz (AZT+3TC+EFZ) were 46(28%) while those on Zidovudine, lamivudine and nevirapine (AZT+3TC+NVP) were 37(22.6%) Stavudine, lamivudine, and efavirenz (D4T+3TC+NVP) group numbered 27(16.5%). Stavudine, lamivudine and nevirapine (D4T+3TC+EFZ) group also numbered 31, giving a percentage figure of 18.9%. Altogether, the four principal first line regimens constitute 86% with the others accounting for 14%. In spite of the difficulty in drawing a correlation between treatment failure and treatment initiation regimen type, one thing emerged clearly, that those patients put on lopinavir/ritonavir based combination produced a much more appreciable rise in CD4 as compared to the others.

Another significant observation was that 26 patients corresponding to 15.9 % of those that benefited from non nucleoside reverse transcriptase inhibitor based regimen had either type 2 or dual type 1&2 infection. For this reason their clinical response was either not realized or unsustainable. The simple reason for this situation is that non nucleoside reverse transcriptase inhibitors are inactive against type 2 HIV. This issue is one of practical importance since it borders on misclassification of patients or misdiagnosis.

5.4.7 Demographic Factors

Data gathered on the educational levels of study participants indicate that 80.5% had either no formal education or had education up to primary level. From the employment figures only 7.9% of the participants were government employees and can be said to have regular source of income. It is therefore highly probable that only a small percentage of the 92.1% of the participants who claim to be unemployed, self employed or employed in the private sector of the economy can be sure of regular source of income due to intermittent episodes of ill health. In such circumstances one can be confident in arguing that a greater majority of the patients had problems with finance and for that matter adherence to therapy which seriously impinges on treatment outcome.

Regarding social or residential status, 28 patients constituting 17.1% were rural dwellers while 134(81.7%) were urban dwellers. This finding seems to corroborate to a large extent the 2008 HIV Sentinel Survey (HSS) Report of Ghana. The report indicates that HIV prevalence in urban areas was higher than in rural areas. The figures quoted in the report indicate that the mean and median prevalence values for urban communities are 2.6% and 2.3% respectively as compared rural value of 2.6% and 2.1% respectively. The wide disparity in percentage figures between Sentinel Survey Report and the KATH values should not in any way be a source of confusion in that while the HSS is contextualized in the general population of Ghanaians, the KATH figures are situated in a population of HIV patients who are actually on antiretroviral therapy.

Once again the study has not been able to establish a very strong link between social standing and antiretroviral treatment failure. However it sounds reasonable to argue that in rural settings where poverty levels are higher, financial constraints can adversely affect access to ART and therefore poor adherence can set in.

The age distribution of the patients is as follows: 17.7% (29) patients belonged to the age group 21-30years, 36.6% (60) patients aged between 31-40 years, 29.9% (49) patients were within the age group 41-50 years. Altogether, 84% (138) 0f the patients were within the age bracket of 21-50. The fact that 84% of the study population belong to the age group 21-50 years is very worrisome. Already, this category of patients are on second line regimen which are characterized by higher pill burden, more side effects, very unfavorable drug-food and drug-drug interactions which make them hard to take. Local research findings are not available to guide us determine how long these patients can be sustained on second line regimen.

Secondly some of these patients have (together with some pediatric patients) given strong indications that they are not doing too well on their new regimen and have been put on salvage therapy. Unless something drastic is done it is likely that more than half of this study population will be lost to the battle against AIDS, probably within the next two to three years particularly if the drug supply situation worsens. Certainly the economic implications of such a loss will be difficult to quantify at this point. It is however relatively easy to imagine the number of orphans and other dependants that

will be left, the skills and expertise that will be lost and their impact on the economy of this country.

Lastly there has not been found any strong association between marital status and treatment failure. The figures indicate that 75 patients among the study population representing 46% are in marital relationships. Fifty four percent are therefore free from marital bonds. Currently there is a concept referred to as “care and support” among persons living with HIV/AIDS within which context some perceived sexual relationships develop. This can facilitate the transmission of resistant strains of virus within PLWHAs, especially among those who are not married and hamper progress of treatment. Beyond this some marital bonds are constantly being formed due largely to a high level of acceptability among PLWHA population. It must be remembered that one of the difficulties pertaining to HIV infection is disclosure of sero-status.

The psychosocial needs of PLWHAs are not different from those of the general population. A few of these include sexual needs, marital satisfaction and the desire to have children. PLWHAs also get motivated by these to establish marital or sexual relationships with people within the general population who may be sero-negative or positive without self disclosure. If they have resistant viral strains, the possibility of transmission of such strains through marriage becomes high.

CHAPTER SIX

RECOMMENDATIONS AND CONCLUSION

6.1 SUMMARY OF RESULTS

Antiretroviral treatment failure among patients receiving care at Komfo Anokye Teaching Hospital is a reality. The study has found that over the last 5 years, prevalence of treatment failure cases is about 3.7%. It was found also that some 7.3% representing 12 patients of the study population had been lost to follow up because of possible death, transfer to other ART sites or treatment default. The fact that 92.7% of these patients are still alive and accessing treatment is a great success to the ART program at Komfo Anokye Teaching Hospital.

The study could not convincingly establish strong association between demographic data such as age, gender, educational background, social standing, employment status, and marital status on one hand and antiretroviral treatment failure on the other. However it was noted that demographic characteristics of participants may have a strong relationship with poor adherence to antiretroviral therapy. Financial constraint was cited by most patients interviewed as the reason for their non adherence to therapy.

6.2 RECOMMENDATIONS

6.2.1 Resource mobilization

As the nation pursues its agenda of scaling up and expanding access to care accrediting more public and private sector healthcare facilities it should be borne in mind that logistics mobilization must be made to move in tandem with infrastructural

development and human resource capacity building. In this regard basic technological aids like CD4 and viral load machines together with the requisite reagents and accessories should be mobilized.

Capacity building of staff in the area of resistance testing must be organized and the necessary technological tools procured. The NACP, GAC and other bodies set up to implement HIV/AIDS related programmes are doing their best but they need to be encouraged and supported in every way possible particularly by government to do much more.

6.2.2 Monitoring

As private sector participation is enlisted with the goal of speeding up access to therapy to a greater percentage of the population, one great challenge is getting private sector workers to adhere to treatment protocols and the general framework of regulations governing anti-retroviral therapy programmes .This is equally applicable in the public sector. Data management and front desk staff at the clinic must be made to recognize and recommend to clinicians the need to effect regimen changes especially when they are equipped with information about patients beginning to fail on therapies.

Additionally the current practice of assessing stable patients' CD4 at six months intervals could be reviewed to three months. It is my belief that when this is done treatment failure can be recognized much earlier and the necessary intervention instituted.

6.2.3 Drug Supply situation

It appears that total reliance on government and donor partners for everything pertaining to HIV/AIDS care is not sustainable on a long term basis with particular reference to drugs. It will be useful to resource and give accreditation to some local pharmaceutical companies to produce equally good quality drugs with proven efficacy for the ART programme at comparatively reduced cost to supplement imported products. Every effort must be made to prevent the occasional shortages of antiretroviral drugs that sometimes affect innocent children for long periods.

Additionally, it must be recognized that the current scope of ARVs present in the country needs to be revised and possibly expanded. Too often doctors, pharmacists and adherence counselors get frustrated due to limitation of choice particularly in times of treatment failure. For this reason I wish to recommend that other products with proven efficacy can be brought in to reduce the level of frustrations.

6.2.4 Improving Adherence to Therapy

Many reasons can be given in support of why patients' adherence to therapy suffers setbacks. These can be categorized into health care provider related, patient related and drug related factors. Drug related factors can be situated in the general context of logistics.In recent times one issue that has engaged the attention of adherence counselors is the claim by herbal medical and religious practitioners that their products offer cure against HIV/AIDS. Some patients on ART interrupt treatment and switch to these products only to come back to the clinic in a worst state than before. It is my firm

belief that advantage could be taken of the current media proliferation to highlight on the gains of antiretroviral medicines with the view of promoting adherence.

This strategy should not in any way replace existing adherence counseling structures in the various health institutions but rather to augment them. In my opinion a platform should be created and offered by government to practitioners who claim to have found cure for HIV/AIDS so that scientific investigations could be conducted into their products and those found to have some level of efficacy assisted to produce to meet international standards. Every effort must be made to identify leaders of such practitioners and given the necessary training to enhance their understanding of HIV/AIDS issues.

6.2.5 Financial assistance to Patients

The current arrangement by which each patient pays a token of five Ghana Cedis per month to access care is a good thing. It must also be emphasized that patients who are unable to pay are not denied access to treatment. Various arguments have been advanced in support of abolishing this payment system, thus making access to care absolutely free as happens in other countries. Counter arguments have been raised to the point that this move is likely to affect adherence to therapy with the explanation that people normally do not value things that they do not contribute anything towards their acquisition.

Secondly, it may not be practicable on long term basis. My personal opinion on this matter is that every effort be made to exempt HIV positive children and parents who are themselves HIV positive together with their children from paying. This will go a long way in reducing the financial burden of parents especially mothers of HIV positive children who have been widowed, or whose husbands have abandoned them and who in most cases are jobless.

6.2.6 Capacity Building and Integration of Care

HIV/AIDS management has become an area of specialty. As we endeavor to scale up access to care to a greater number of our population, it will be needful to think of integrating care with other health conditions like malaria, hypertension and others. This will even help to reduce stigma associated with HIV infection. For this reason it will be important to design and incorporate HIV management oriented programs into the curricula of all health related educational institutions with the objective of equipping health professionals beforehand. Again more health workers in the various health institutions must be given the opportunity to train and update their skill in this regard.

6.3 CONCLUSION

In conclusion I would like to appeal to all and sundry to pool the neccesary resources together in combating HIV/AIDS. In the USA, few cases were identified during the early 1980s. In Ghana, the first case was reported in 1986. Other places have their own stories to tell. No matter what stories can be told, the one greatest story is that HIV/AIDS is a global issue. In the same way the few initial cases have assumed global

dimensions, the few resistant and therefore treatment failure cases have the potential to translate into epidemic or pandemic proportions if nothing drastic is initiated. If we allow this to happen we stand the chance of losing the battle against HIV/AIDS. The reason is simple. It is much easier to prevent the development of drug resistance than to manage treatment failure cases.

Before I finally end it all, I would like to identify with the World Health Organization on some four basic facts about ART as quoted below:

"No antiretroviral drug is resistance proof, HIV drug resistance will evolve naturally, when confronted by the selective pressure from drugs or from the immune system. When HIV is not fully suppressed, drug resistance ultimately results. This situation is frequently linked to non-compliance of ARV therapy. Resistant viruses can spread and affect ARV therapy, transmission of HIV resistance strains is of increasing concern in countries where ARV is widely used. Resistance can be contained; the likelihood of its occurrence can be reduced or prevented by an appropriate and careful choice of treatment and by monitoring for resistance."

This is the responsibility of all persons involved in the fight against HIV/AIDS.

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APPENDICES

Appendix 1

PREVALENCE AND CAUSES OF ANTIRETROVIRAL TREATMENT FAILURE AT KATH

Data collection Tool

Study I. D No……

Facility Unique No……..……..

Age……...……

Sex……...…….

ART start Date……...……..…….

CD4+ at ART initiation……...……..…..……

ART initiation regimen……...…….

Peak CD4+……...……

Date of Change……..……

Second line regimen……..……

Duration on First line……...

Reason for change……

Clinical conditions/symptoms of failure……..……

……..……

……..……

Comments…….……

Appendix 2

PREVALENCE AND CAUSES OF ANTIRETROVIRAL TREATMENT FAILURE AT KATH

PARTICIPANTS' CONSENT STATEMENT

Hello, my name is Rev. Raphael Kweku Obeng. I am a member of the clinical care team of Komfo Anokye Teaching Hospital that offers antiretroviral therapy to persons living with HIV/AIDS. I am carrying out a research into the causes and prevention of antiretroviral treatment failure as part of my project work towards the award of M. Sc. Clinical Pharmacy degree at the Kwame Nkrumah University of Science and Technology. I wish to interview as many people as possible who have failed on their first line regimen. I have found out that you are eligible to participate in the study. I would therefore like you to be one of the respondents. You are at liberty to decide whether to be part of the study or not. Your failure or refusal to participate will not in any way affects the quality or level of care you do currently receive at the clinic.

Should you decide to participate in the study, you will not receive any direct benefit in terms of monetary or material gain. However, since the purpose of the study is to gain insight about treatment failure and how to prevent it, you will receive indirect benefit of enhanced clinical care in order for you to stay much longer on your current second line regimen.

I would like to assure you of a high level of confidentiality. Any information taken from you will be coded and jealously guarded in order not to expose you to undue risk of stigmatization and discrimination. If I discover in the course of the study that you need a certain level of care which you are currently not receiving, I will endeavor to discuss your matter with any person who can provide that particular service or care. In such circumstances, the matter will be discussed with you and your consent expressly sought before the necessary intervention. If you now agree to participate in the study, I would like you to indicate that by signing below as I am going to do.

Researcher's signature_____ Date_____

Participant signature_____ Date_____

Patient's I.D. No._____ Study I.D. No._____

Appendix 3

PROJECT QUESTIONNAIRE

A. Demographic data

1. Age: (a) 18-29 (b) 30-39 (c) 40-49 (d) 50-59 (e) 60-69 (f) >70

2. Sex: (a) Male (a) Female

3. Marital status: (a) married, (b) widowed, (c) single,

(d) divorced/separated, (e) Never married

4. No. of children: (a) one (b) two (c) three (d) four or more (e) none.

B. Infection history

5. Infection awareness history

For how long have you known you are infected with HIV?

(a) <1yr (b) 2-4yrs (c) 4-6yrs (d) 7-10yrs

6. How did you become aware of your HIV status?

(a) Diagnostic (a) VCT (c) PMTCT (d) Other……

7. Infection source perception

Looking back in history, how do you think you acquired the infection?

(a) contaminated instruments (a) blood donation (c) heterosexual contact

(d) homosexual contact (e) witchcraft (f) can not tell

8. Pre-diagnosis treatment history

Before you were diagnosed HIV positive did you receive treatment for some conditions that suggested to you that you were ill? Yes or No

9. What kind of illness was it?

(a) RTI (b) STD (c) skin diseases (d) GIT conditions (e) other……

10. Where did you receive such treatment?

(a) hospital (b) herbalists/traditional healer (c) spiritualist (d) prayer camp (e) other

C. ARV previous exposure history

11. Did you receive antiretroviral medicines at that facility? Yes or No

How many HIV/AIDS medications did you take at a time? (a) one (b) two (c) three

12 Did you receive regular supplies of antiretroviral medicines? Yes or No

Can you tell me about the source of the drugs?

(a) local market (b) ordered (c) relatives abroad (d) other(s)……

13. Were there times that you did not receive ARV drug supplies? Yes or No

If yes, what was (were) the problem(s)?

(a) availability (b) affordability (c) staff attitude (d) other……

14. I would like you to tell me how you paid for clinical services.

How much did you pay monthly on the average? .....

How did you pay for the services and drugs? …….

Were there times you could not afford to pay due to lack of resources? Yes or No

Assessing adherence to therapy at KATH

15 For how long have you been on treatment at KATH?

1yr 2yrs 3yrs 4yrs 5yrs other……..

16. Have you had treatment interruption at KATH before? Yes or No

If yes, how often did it happen?

(a) once (b) twice (c) three times or more…..

20. What was the duration?

(a) one week (b) two weeks (c) eight weeks or more (d) other…….

17. What made you interrupt your treatment?
    (a) illness (b) distance (c) financial (d) other ……

18. Is there anything that makes it difficult for you to take your medicines? Yes or No.
    If yes, what is it?
    (a) pill burden (b) side effects (c) dosage frequency (d) other……..

19. Have you missed appointment with your doctor before? If yes, what is the reason?
    (a) distance from clinic (b) financial (c) lack of reagents at lab. (d) other…….

20.How many times has it happened? (a) once (b) twice (c) three or more…..

21. Now I would like you to make some comments regarding your treatment at KATH
    Location of the clinic promotes confidentiality. True or False

22. Services rendered by:
    Counselors, (a) appreciable (b) not appreciable (c) other……..
    Nursing staff, (a) appreciable (b) not appreciable (c) other……..
    Doctors, (a) appreciable (b) not appreciable (c) other……..
    Pharmacy staff, (a) appreciable (b) not appreciable (c) other……..

23. Cordiality of staff, (a) appreciable (b) not appreciable (c) other……..

Appendix 4

Data Summary Sheet

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	
1							Appendix 4								
2				PREVALENCE AND CAUSES OF ANTIRETROVIRAL TRETMENT FAILURE-PROJECT SUMMARY SHEET											
3	UNQ. NO.	SEX	AGE	HIV TYPE	IST LINE	DUR/MTHS	START CD4	PEAK CD4	DIFF	PKT/MTHS	% INC	PREV EXP.	ADHR.	COMMENT	TB
4															
5															
6															
7															
8															
9															
10															
11															
12															
13															
14															
15															
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