FACTORS INFLUENCING ANTIRETROVIRAL TREATMENT FAILURE AMONG ADULT HIV PATIENTS AT BOMU HOSPITAL MOMBASA COUNTY

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Factors Influencing Antiretroviral Treatment Failure Among Adult HIV Patients at Bomu Hospital Mombasa County

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DECLARATION

This thesis is my original work and has not been presented for a degree award in any other University

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This thesis has been submitted for examination with my approval as University Supervisor.

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DEDICATION

I dedicate this thesis to my parents, my loving wife and children, for their patience and support during my postgraduate studies. It was a difficult time managing family matters, studies and my job.

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ABBREVIATIONS AND ACRONYMS

3TC Lamivudine

ABC Abacavir

ADR Adverse Drug Reaction

AIDS Acquired Immune Deficiency Syndrome

ART Antiretroviral Therapy

ARV Antiretroviral

ATV/r Atazanavir/ritonavir

ATV Atazanavir

AZT Azidothymidine

CD4 Cluster of Differentiation Type 4

CI Confidence Interval

CVS Cardiovascular System

DALY Disability Adjusted Life Years

D4T Stavudine

DRV/r Darunavir/ritonavir

EFV Efavirenz

HAART Highly Active Antiretroviral Therapy

HIV Human Immunodeficiency Virus

HTG Hypertriglyceridemia

KASF Kenya AIDS Strategic Framework

LPV/r Lopinavir/ritonavir

LPV Lopinavir

NACC National AIDS Control Council

NACOSTI National Council for Science and Technology

NASCOP National AIDS/STD Control Program

NNRTI Non Nucleoside Reverse Transcriptase Inhibitor

NRTI Nucleoside Reverse Transcriptase Inhibitor

NVP Nevirapine

NVP Nevirapine

PEPFAR U.S. President's Emergency Plan for AIDS Relief

TDF Tenofovir disoproxil fumarate

UNAIDS United Nations Program on HIV and AIDS

VF Virological Failure

WHO World Health Organization

DEFINITION OF TERMS

Adherence- It refers to the extent to which patients follow the instructions of their health care provider with respect to taking their dugs

DALY's - means Disability Adjusted Life Years – Time lost due to incapacity arising from ill health.

Treatment Failure – For the purpose of this study, this has been defined as a one - off plasma viral load ≥ 1000 copies/ml

First Line ART treatment- It is the initial combination of antiretroviral drugs prescribed for an eligible HIV infected patient who has not taken any ARV before

Second line ART treatment – It is the combination of antiretroviral drugs given to a patient after first line fails to suppress HIV replication

ABSTRACT

Bomu Hospital is one of the sites in Mombasa which started providing antiretroviral therapy (ART) to HIV-infected patients since 2004. At this hospital, as in other sites, there are an increasing number of patients requiring a switch from first line to second line ART drug regimens due to treatment failure. The objective of this study was to determine the factors that influence ARV treatment failure among adult patients under treatment at Bomu Hospital. The study was cross sectional at initial patient recruitment and retrospective for patient level data. Two hundred and ninety nine study participants were selected from a total of 18 425 active on ART. Convenient sampling technique was used to select the adult population for study and thereafter it was categorized into two groups. Those with one - off plasma viral load of ≥ 1000 copies per ml were termed as failing treatment while those with less than 1000 copies per ml were termed as responding well to treatment. Semi-structured interview schedules were used to obtain demographic information and patients' views on various dimensions of ART services at the hospital. The study discussed several broad areas related to antiretroviral treatment failure, including finding out the socioeconomic and sociodemographic patterns of adult patients under ARV treatment at Bomu Hospital. This study also determined the duration at which the patient has been on ART and the development of treatment failure. The study compared the failure rate of ARV to Co infections and the relationship of viral load and CD4 counts on patients on ART. Fisher's exact tests and unpaired t-tests were performed to compare clinical and laboratory characteristics according to viral load screening status. Multiple logistic regression attempts was used to determine the factors which can predict treatment failure and hence useful models for prediction of treatment failure can be used for decision making. Using Chi square test of independence (Fisher exact test) it was found that there was significant association at 5% level of significance between viral suppression and some of the social demographic factors namely marital status and age groups. Using multiple logistic regression model to determine which social demographic and social economic factors affect viral suppression, it was found that age groups and marital status are statistically significant at 10% and 5% respectively. The elderly had a complete viral suppression (88.2%) compared to the young while the married people had a complete viral suppression (p value 0.003) compared to other segment of marital status. The results showed that there was no significant relationship between period of treatment, co infections and viral suppression. There was significant relationship between the viral suppression and current CD4 count (p value 0.000). The viral suppression was higher among those with high CD4 count. Bomu Hospital had an overall viral suppression of 76.9% compared to the national target of 90% hence concerted efforts required to identify patients, the youth and young adults with high viral load at higher risk of treatment failure.

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Globally, HIV is a public health concern which has claimed more than 39 million lives so far, (UNAIDS,2013). In 2013, between 1.4 to 1.7 million people died from HIV-related causes. By the end of 2013, approximately 35.0 million people were living with HIV. New infections ranged between 1.9–2.4 million (UNAIDS 2013). The region most affected is Sub-Saharan Africa with 24.7 million people living with HIV, accounting for almost 70% of the new infections globally (WHO, 2010).

The presence of HIV infection is usually diagnosed through blood test which detects the presence or absence of HIV antibodies. As there is currently no cure for HIV infection, effective treatment with antiretroviral (ARV) drugs can only control the virus multiplication so that people with HIV can enjoy healthy and productive lives. People on antiretroviral therapy was 12.9 million (ART) globally (UNAIDS, 2012). In this population 11.7 million were from low and middle income countries, representing 36% (34- 38%). In children, HIV treatment and care was slow in low and middle income countries where less than 1 in 4 children who were infected with HIV had access to ART, compared to over 1 in 3 adults (WHO, 2010).

In Kenya, between 1995 and 1996, the general population had an HIV prevalence of 10.5% which declined to 6.7% in 2003. The epidemic then stabilized to 5.6% in 2012 (NASCOP, 2012). The stabilization was due to an increased HIV treatment and care, though the reduction of new infections was small (Kenya, 2009). The 2011–2015 UNAIDS strategy set country targets in accessing HIV prevention, treatment and care services thereby reducing the HIV epidemic aimed at achieving the Millennium Development Goals (MDGs) by 2015.

In Kenya, between 2003 – 2011 approximately 400,000 individuals had been started on ART in the country, (NACC and NASCOP, 2012). The increase in number of people who could access ART resulted in the decline in HIV incidence, morbidity and mortality (Bendavid and Bhattacharya, 2009; Jahn et *al.*, 2008; and UNAIDS, 2013).

The health of HIV infected population improved with the use antiretroviral therapy (ART) (Palella *et al.,* 1998). The development of antiretroviral therapy in the form of Highly Active Antiretroviral Therapy (HAART) substantially reduced AIDS-related morbidity and mortality (Ledergerber *et al.,* 2004). To date, ART has been based on a combination of drugs from two of the three original classes; non-nucleoside reverse transcriptase inhibitors (NNRTIs); nucleoside reverse transcriptase inhibitors (NtRTIs); and protease inhibitors (PIs). The key indicators of the degree of success of the national ART program relies on the proportion of patients on therapy that achieve HIV viral load suppression to lower than detectable levels and attain a CD4 count more than 350 cells/ mm (Finzi *et al*.,1999).

Initially the natural history of HIV infection directly lead to acquired immunodeficiency syndrome (AIDS) and death, and the efficacy of treatment was determined by its ability to delay this fast progression (Paredes,2000). HIV treatment started with the use of one antiretroviral drug and then dual therapy. It was only in 1996 that a combination of three antiretroviral drugs could achieve an undetectable viral load was realized (Palella *et al*., 1998).

The clinical prognosis of HIV infection has changed because of the widespread use of HAART (Paredes, 2000). The goal of antiretroviral therapy is to reduce and maintain HIV – 1RNA levels below the lowest detectable level (Hirsch *et al*., 1998). As the duration of infection increases, however, the mortality rate among HIV-infected patient's increases compared with the general population (Yazdanpanah, 2009). This long-term excess mortality is likely to persist because antiretroviral therapy -related

toxicity, non-adherence, and drug resistance, which may lead to treatment failure, are likely to increase with time on combination with antiretroviral therapy.

There are three kinds of treatment failure namely: clinical failure, immunological failure and virological failure. Many patients have had multiple episodes of virological failure; especially those were who initiated with one or two nucleoside therapy before the introduction of HAART, (Bansi *et al.,* 2010). Studies have shown that the lowest HIV-1 RNA levels are required to achieve a durable virological response. Durable virological and immunological responses are required to improve the clinical prognosis of patients (Paredes, 2000). Evaluating the patients who have experienced treatment failure is important for understanding the success of ART.

In Kenya, ARVs are offered for free in all government health facilities, some faith based hospitals and selected private facilities and other nongovernmental organizations such as Bomu Hospital. After 10 years of provision of ART at the Bomu Hospital, it is useful to evaluate and analyze the data available for relationships and trends of patients failing treatment, in order to make informed and useful policy and operational decisions to improve and strengthen existing ART systems. Of potential importance may be the factors that influence the poor outcome of therapy in patients on ART.

1.2 Statement of the Problem

Although there is a reduction in HIV/AIDS mortality globally, it is still ranked fifth leading cause of global DALYs (Sigaloff *et al.*, 2013). The suffering in patients with HIV/AIDS burden is not equal in regions and demographics. In the four world blocks namely Caribbean, Thailand, Eastern, Southern Africa and Central Africa, adults who ranged between 30 - 44 years living with HIV/AIDS had the highest DALYs (Delate and Coons, 2001).

The use of antiretroviral treatment has led to the increase in life expectancy to almost the general population (Ashford, L. 2006). Other studies have also shown that since the introduction of ART, mortality rates among PLWHA have become almost the same (Campsmith *et al.*, 2003; Goldman *et al*., 2008; Nakagawa *et al*., 2012; Mills *et al*., 2011). However little has been reported on the causes of antiretroviral treatment failure which are site or region specific or even among clients with good adherence.

While these studies have shown improved clinical outcomes of PLWHA, information about the different factors that influence antiretroviral treatment failure and how chronic management of HIV/AIDS has affected their lives is rare. People infected with HIV expect to get treatment that will make them live long and also improve the quality of their lives (Delate and Coons, 2001).

In Kenya, life expectancy for people with HIV/AIDS is unknown and what proportion of the life lived is good health. With inequalities recorded across Kenyan population in almost all health indicators, it is not known if the same pattern can be expected for health adjusted life expectancy among HIV/AIDS patients and what factors explain differences in treatment outcomes among clients put on antiretroviral therapy. Loss of life in HIV patients who were on ART is sometimes unexplainable as care and treatment chain starts with testing, counseling, periodic monitoring to achieve a complete viral undetectable level.

The focus of this study was to determine antiretroviral treatment outcome among PLWHA and thereby understand the possible factors that could contribute to treatment failure even among those clients with good adherence. Reasons for continued health losses to HIV when ART is widely available are poorly understood. The care cascade describes the series of engagements with the health system through which people with HIV must pass to benefit fully from ART, beginning with HIV testing, and ending with regular monitoring of patients in a state of sustained viral suppression.

There are still many unresolved issues associated with good treatment outcome, such as the ability of patients to tolerate the treatment, drug toxicity, resistance and available treatment options. Studies have shown that some newly infected patients already have mutant HIV which are not susceptible to the available ARVs (Messou *et al.*, 2011).

1.2.1 Problems related to antiretroviral treatment

ARV treatment is a lifelong therapy thus is useful to understand features of the virus, the ARVs and the patient. All these factors put together directly impact the lifelong treatment.

Viral Multiplication

The HIV multiplies at a rate of approximately 10^{10} copies per day and in the process mutant viruses are made (Kuritzkes *et al.*, 2008). Mutant viruses are the cause of viral resistance (Paterson *et al.*, 2000). Undetectable viral level is often achieved after 6-12 months of treatment; however, in other body secretions such as seminal fluid, the virus can be detectable (Finzi *et al*., 1999).

Stopping antiretroviral treatment follows a process of virus multiplication due to potential 'reservoirs', which are immune cells infected with the HIV but not making new copies of virus. (Boyd and Cooper, 2007). Different drug combinations have been used to treat the drug resistant viruses but the usefulness of such treatment option has not been seen (Boyd, Emery, and Cooper, 2009). Resistance to drugs in patients who have been on long term treatment have also been seen (El-Khatib *et al*., 2011).

Effects of ARV Drugs

Drug concentration does not reach the required levels to eliminate the virus from the reservoir. ARVs are known to be toxic which further complicates treatment since this causes serious drug reactions (Gutierrez *et al*., 2006). Increased levels of triglycerides have been reported on patients using HAART for longer period (Cornell *et al.*, 2010). High levels of triglyceride results in the risk of heart and brain diseases in patients on ART (Bartlett, 2002). Drug to drug interaction which is significant on patients on ART inhibits cytochrome P450 (CYP450) isoenzyme, as this enzyme affects other different types of drugs (Galai *et al.*, 1997, Gebo et *al.*, 2005).Integrase inhibitor, raltegravir is metabolized by UGT1A1 mediated glucoronidation which slightly interacts with CYP450 enzymes, while elvitegravir which is metabolized by CYP3A4 (Mocroft *et al.*, 2010). Treating HIV patients with opportunistic infections by use of other non HIV drugs including use of herbal medication affects the management of HIV patients (Lifson *et al.*, 2010).

It is known that to suppress the viruses to undetectable levels, the best practice is to use three or more drugs from the different classes of ART, followed by good adherence. This however leads to high pill burden and accumulation of toxicities (Paterson *et al.*, 2000).

Failure to reduce the viruses to undetectable levels occur due to resistance especially in poor countries where there are few treatment options and lack of adequate facilities to monitor drug reactions and accessible monitoring facilities (Bhaskaran, 2008).

Patient conditions

Adverse drug reactions might develop in patients who are already suffering from other medical conditions such as liver disease, diabetes, kidney disease, mental condition etc. hence such patients require special attention. The development of co infections such as tuberculosis furthermore increases more pill burden, more chances of bad drug interactions with increased toxicity. Such complications make it difficult to classify whether these problems are due to toxic levels of ARVs, drugs for other conditions or the virus itself as these may present with similar signs and symptoms (Paterson *et al.,* 2000). .

Patients on HAART have been reported to live long (Glick and Sahn, 2008). The elderly population is at risk of other diseases such as heart disease (Little *et al.,* 2002). This in turn brings challenges on the selection of appropriate medication for diseases such as high blood pressure together with ARVs. Pregnant women for example may require special dose combination. All these factors need mutual understanding and relationship between the patient and caregiver which might be difficult in poor resource settings and in countries which are still developing.

1.3 Justification

The quality of life for people living with HIV/AIDS has improved following the introduction of HAART hence has reduced the suffering and death. The introduction of HIV Counseling and Testing (HCT) campaign by the Kenyan government, more people have come to know their status and started on antiretroviral therapy. Access to HIV prevention, care and treatment increased with the UNAIDS 2011 -2015 strategy. However, core to the success of this program is the durability of antiretroviral therapy. Inability to sustain treatment may lead to treatment failure and hence defeat the purpose. First line therapy may fail if patients drug adherence patterns are not followed resulting to formation of resistant strains thus change in therapy to the second line. In developing

countries and resource limited settings, the classes of antiretroviral drugs available are limited. Kenya has reported an increase in patients started on ART, however to retain patient on treatment for longer periods especially those who are lost to follow up has been of great concern (Cornell *et al.*; 2010).

A continuous and sustained suppression of viral replication is required for prolonged clinical benefit (Little *et al.,* 2002). Suboptimal viral suppression often leads to drug resistance and subsequently treatment failure and spread of resistance strains. Occurrence of treatment failure often has socio-economic implications because of the increased direct and indirect cost associated with starting expensive second line regimen. Improvement of patient outcome is dependent on putting the patients on successful regimes (Paterson *et al.,* 2000). Knowledge of factors that are predictive of treatment failure will aid in isolating patients that are at a higher risk of treatment failure. Furthermore, in absence of predictive factors, the scarce resources available may be wasted unnecessarily by using it for patients that are less likely to develop treatment failure (Basenero *et al*., 2007).

This study provided valuable information about the clinical progression of patients on ART. It sought to identify specific issues requiring attention from service providers and policy makers while providing scientific foundation for practical patient-friendly recommendations. Durability of virological response is one of the goals to improve the clinical prognosis of patients; hence monitoring the proportion of patients with failing treatment assists in developing successful antiretroviral therapy regime. Understanding the proportion of patient failing treatment will also help in clinical decision making such as strengthening treatment adherence by counselors and support groups. This study utilized variables that are routinely measured in the clinic specifically HIV viral load and CD4 count in order to determine treatment failure. Routine variables that are routinely collected such as the distance travelled to the clinic, WHO stage, age, gender and presence of concomitant disease, were also assessed to find out if there is a relationship between treatment failure and these variables

1.4 Research Questions

1) What are the socioeconomic and sociodemographic patterns of adult patients under ARV at Bomu Hospital?
2) Does prolonged use of ARVs results into treatment failure?
3) What is the relationship between co-morbidities and ARV treatment failure?
4) What is the relationship between viral load and CD4 + T cells count?

1.5 Objectives

To determine factors that influence ARV treatment failure among adult clients on follow up Bomu Hospital, Mombasa County.

1.5.1 Specific Objectives

1) To determine the socioeconomic and sociodemographic patterns of adult patients under ARV treatment at Bomu Hospital
2) To determine the relationship between prolonged use of ARVs and treatment failure.
3) To determine the relationship between co-morbidities and ARV treatment failure.
4) To determine the relationship between CD4+ T cells count and viral loads on patients on treatment

1.6 Scope

Adult patients on ARVs were enrolled into the study. These were patients seen at the Clinic during their routine clinic visit and are on first or second line treatment. These patients were on ARVs for at least one year. The study was conducted at Bomu Hospital.

1.7 Limitation

The major limitation of the study was the inability to do drug resistance that could help understand the class of drugs which were resistant and to detect mutations in the viral genomes in plasma samples due to lack of necessary equipment.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Antiretroviral therapy (ART) has improved the wellbeing of people infected with HIV (Palella *et al*., 1998). Morbidity and mortality has gradually decreased following the introduction of Highly Active Antiretroviral Therapy (Lozano, Ortblad, Lopez, and Murray, 2013). HIV is nowadays treated by use of a combination of two classes of the three classes of ARVs namely; non-nucleoside reverse transcriptase inhibitors (NNRTIs); nucleo (t) side reverse transcriptase inhibitors [N (t) RTIs]; and protease inhibitors (PIs). Patients who achieve undetectable levels of virus with a CD4 count greater than 350 cells/mm^3 indicate a high level of success in any national or regional ART program (Perrin, 1998).

Initially, infection with HIV slowly and directly led to acquired immunodeficiency syndrome (AIDS) and loss of life. Good treatment outcome is seen when the disease progression is delayed. Single drug treatment was first started then later in 1996, three antiretroviral drugs were introduced which achieved complete viral suppression (Paredes *et al*., 2000). High viral load is linked to disease progression, while the aim of antiretroviral therapy is to lower and maintain the viral load to undetectable levels (Hirsch *et al*., 1998). As the duration of infection increases, however, the mortality rate among HIV-infected patient's increases compared with the general population (Yazdanpanah, 2009). This long-term excess mortality is likely to persist because antiretroviral therapy related toxicity, non-adherence, and drug resistance, which may lead to treatment failure, are likely to increase with time on combination of antiretroviral therapy.

Patients at risk of failing treatment are those initiated with single or two nucleoside treatment before the introduction of HAART (Bansi *et al.,* 2010). Undetectable viral load is required to obtain a good long term treatment outcome, which is the goal of a prolonged immunological and virological response (Paredes, 2000).

The first line treatment for new patients' treatment including pregnant women is TDF+3TC/EFV. This however can be alternated with TDF+ 3TC+NVP, AZT+3TC+EFV, AZT+3TC + NVP. ABC+3TC+ EFV is recommended for patients with renal disease. For Abacavir (ABC), no dose adjustment is required (NASCOP, 2011). Strict adherence is required during the first line management. Viral load greater than 1000 after 3 months of ART for a patient with strict adherence qualifies to be changed to second line.

Second line treatment for adults and adolescents is AZT+3TC+ATV/r or alternate second line ART regimen of AZT+3TC+LPV/r. The recommended second line treatment for patients initially AZT+3TC+EFV/NVP or D4T+3TC+ EFV/NVP, is TDF+3TC+ATV/r, which can alternate with TDF+3TC+LPV/r. patients on TDF/3TC+ATV/r/LPV/r should be switched to AZT+3TC+DRV/r. The recommended Protease inhibitor (PI) for new patients on second line is ATV/r. (NASCOP, 2012). First and second line treatment in adolescents and adults can be summarized in the table 2.1.

Table 2.1: First and Second line treatment in adolescent and adults

First Line ART in Adolescents and Adults		
	Preferred regimen	**Alternative regimen**
First line ART regimen for adolescents (≥15 years) and adults	TDF+3TC+EFV	TDF+3TC+NVP AZT+3TC+EFV AZT+3TC+NVP
First line ART regiment for HIV infected sexual partner in a sero –discordant relationship	TDF+3TC+EFV	TDF+3TC+NVP AZT+3TC+EFV AZT+3TC+NVP
Second Line ART in Adolescents and Adults		
If First line ART regimen	Preferred Second line ART	Alternate Second line ART regimen
TDF+3TC+EFV	AZT+3TC+ATV/r	AZT+3TC+LPV/r
AZT+3TC+EFV/NVP D4T+3TC+EFV/NVP	TDF+3TC+ATV/r	TDF+3TC+ LPV/r
TDF+3TC+ATV/r/LPV/r	AZT+3TC+DRV/r	-

Source: NASCOP 2012

2.1.1 What is Treatment Failure?

This is when the response to treatment with antiretroviral drugs fails to suppress the virus to undetectable levels (NASCOP, 2011).

2.1.2 Types of treatment failure

a) Virological Failure – is defined as having a viral load greater than 1000 copies per ml despite intensive adherence. In this study a onetime viral load greater than 1000 copies per ml was used to describe treatment failure for patients on ARVs for a minimum period of one year and above. The first form of treatment failure often seen is virological. These patients usually progress to immunological failure if they do not change the desired regimen. Immunological failure may be followed by clinical failure (NASCOP, 2011).

b) Immunologic Failure – Is the failure of CD4 cells to increase below 30% of the maximum CD4 count after initiation of therapy, or a continuous CD4 level below 100 cells/mm^3 (NASCOP, 2011).This usually occurs as a consequence of virological failure but can also occur even after suppression of the virus (Bartlett, 2002). In addition other reasons for immunological failure can be due to old age, failure of the thymus to produce more CD4 cells or underlying malignancy.

c) Clinical Failure – This is evident when new, recurring or opportunistic infections or symptoms such as underweight, tiredness and excessive sweating (NASCOP, 2011). Clinical failure is not a good indicator of treatment failure as it follows so long after virological failure.

2.1.3 Factors that may cause treatment failure

Poor adherence: This is when a patient is not taking the prescribed drugs on time and the correct dose. Poor adherence can be due to side effects, the number of pills given and the restrictions to food (Bartlett, Cheever, Johnson, and Paauw, 2004).

Drug resistance: This is when the antiretroviral drugs cannot suppress the virus multiplication. This can occur due to mutation of the viruses or when a patient is infected with a resistant strain initially on HAART (Wittkop *et al*., 2011). Secondary resistance occurs on patients already on ART. This mostly occurs due to inadequate drug concentration and when patients are non-adherent, suboptimal dosing, malabsorption, or drug interactions.

Pharmacokinetics: Drug absorption, distribution, metabolism must be optimal for a successful treatment plan. Different antiretroviral drugs have different absorption rates hence can lead to treatment failure (Wittkop *et al*., 2011).

Co-Morbidity: This is the presence of medical conditions other than HIV infection. Concurrent use of medications for this condition and antiretroviral may lead to additive side effects or drug interactions (Zhou *et al*., 2009).

Inappropriate choice of antiretroviral agent: Taking suboptimal treatments that were available before the current regimen such as monotherapy (single dose of Nevirapine) and dual-therapy of antiretroviral drugs (Wittkop *et al*., 2011).

Inadequate or inconsistent drug supply: This can lead to suboptimal treatment levels in the body. National and funded programs ensure a consist supply throughout the country (Zhou *et al*., 2009).

2.1.4 Diagnosing treatment failure

The viral load test is used to estimate the amount of viruses in blood plasma whereas CD4 checks the immune system of an individual. Different people respond differently following HIV infection.

2.1.5 Switching of ART regimen

Substituting all three drugs is made when there is virological failure. It is not recommended to change treatment when immunological failure occurs in the absence of virological failure. Appropriate laboratory investigations together with good clinical judgment may be required before a patient is changed to a second level treatment (NASCOP, 2012).

2.1.6 The rate of change of CD4 count and viral load

The viral load is expected to reduce gradually to undetectable levels after initiation of ART and this indicates suppression of viral replication (Viard *et al*., 2001). Conversely, the CD4 count is expected to increase gradually after initiation of ART and this signifies immune recovery (Choi, 1993). The rates of change of CD4 count and viral load in an individual have significant prognostic value in determining the time of progression to treatment failure and the durability of treatment (Teixera *et al.,* 2001). Surrogate markers can be used as predictors for the outcome of HIV infection and may provide guidance for initiation or change in antiretroviral therapy (Henrard, 1995). The rate of change of the viral load may be clinically useful as an important predictor of outcome such as predicting sustained virological response to treatment (van Sighem *et al*., 2008).

2.2 Theoretical Review/ Conceptual Framework

Four interacting factors have been hypothesized to influence or determine treatment failure: poor adherence, high viral load, persistent and reduced CD4 count in the presence of treatment, sociodemographic and socio-economic factors and prolonged ARV treatment. This study is set to investigate the factors that substantially lead to ARV treatment failure.

Figure 2.2 gives a scheme of concepts or variables which were operationalized in order to achieve the set objectives.

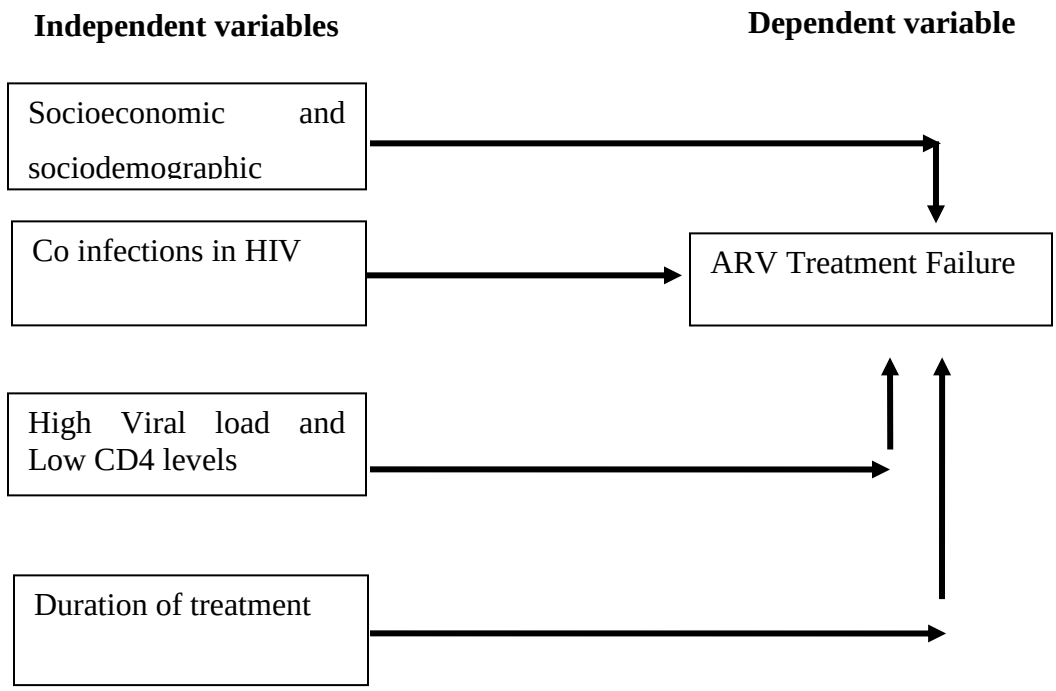

Figure 2.1: Factors influencing ARV treatment failure

2.2.1 Socioeconomic and sociodemographic factors in HIV treatment failure

Little is known about the socioeconomic imbalance among countries with low and average income. In mid 1990s higher HIV prevalence was seen among the educated and wealthy individuals (UNAIDS 1998). Poor living standards, poverty, poor access to adequate healthcare services have attributed to early disease detection which is evident in majority of countries in sub Saharan Africa. In this study, education, employment and income levels including demographics was checked so that a clear picture could be seen if this could contribute to treatment failure.

2.2.2 Duration of ARV treatment and treatment failure

After the initial treatment the sequential treatment strategy is both adaptive and reactive as subsequent regimen change always depends on response to current regimen, medical history, as well as tolerability and toxicity of treatment (Wittkop *et al*., 2011). In clinical practice, patients have historically been given treatment choices to sustain virus suppression, maximize adherence, and minimize toxicity which will result in improved clinical health and long-term survival (Robbins *et al*., 2007). The negative aspects of staying on a failing regimen are counterbalanced by a patient who may be clinically stable for a prolonged period of time and tolerating their initial regimen despite low levels of viral replication (Robbins *et al*., 2007). A final layer of complexity follows from the fact that switching therapy is no panacea to improved intermediate or long-term clinical endpoints (Robbins *et al*., 2010). Patient-specific genetic and environmental factors preclude the existence of a single resolution to a complex disease and, hence, switching ARV therapies may not reduce toxicity nor improve tolerability but lead to problems with adherence (Nachega *et al*., 2006). This study aimed to estimate the duration of ARV treatment and the development of treatment failure response for particular ARV treatment sequences and to compare these sequences using the observed clinical data.

2.2.3 Concomitant disease and medication effects on treatment failure

Opportunistic infections (OIs) are the most significant complication of HIV infection (Feachem, 2004). OIs cause substantial morbidity in HIV infected patients leading to increased economic burden and social burden (Stadeli, 2012). Although success has been achieved through the use of antiretroviral therapy (ART) a large number of individuals living with HIV infection do not maintain viral suppression and thus remain at risk for opportunistic infections (Barth, Tempelman, Morab and Hoepelman, 2011).

Tuberculosis, fungal infections, hepatitis and malaria are common opportunistic infections among patients living with HIV. The study sought to understand whether these opportunistic infections are linked to the risk of developing treatment failure.

2.2.4 Relationship between treatment failure and CD4 - viral - load counts.

High viral load and low CD4 count are independently associated with mortality (Hargreaves *et al*., 2008). Patient who attains a successful viral suppression is expected to improve immunologically. This is in relation to the fact that viral failure often follows immunological failure. Changes in CD4 cell count do not accurately predict suppression of viral load (Finzi *et al.,* 1999). The study measured the viral load and CD4 among patients on antiretroviral therapy for more than one year so as to understand if there was a relationship between virological failure and immunological failure.

2.3 Critique of the existing literature

Poor adherence might be mediated by several factors that may not be openly disclosed by the patients such as use of herbal medication together with ARVs, use of alcohol and cigarette smoking along with other rare medical conditions such as presence of prevalent tropical diseases and lifestyle conditions. Differences in definitions and classification of ARV treatment failure, study designs and population, and methods of statistical analysis might explain these inconsistent results.

2.4 Summary

Various approaches for identifying treatment failure need to be identified since clinical, virological and immunological criteria may not be sufficient. This will avoid incorrect or delayed early or delayed switching of patients to second line regimens. Viral testing is not yet widely available for monitoring of patients on ART in resource poor settings and no other simple tools for treatment failure detection. 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.

2.5 Research gaps

The literature review shows that ARV treatment failure has been studied from many disciplinary perspectives over the last 30 years. These studies present a diverse picture on the treatment outcomes around the globe each with its own characteristics. Such a study has not been conducted in Mombasa.

CHAPTER THREE

METHODOLOGY

3.1 Research Design

A cross sectional study design was adopted at initial patient recruitment. It examined a patient at one point in time. It was useful for descriptive information, screening and estimation of use of services. At this point blood collection was done after a patient interview. A retrospective cohort study design for data obtained from patient records, MOH-recommended medical records onto tailor made data capturing tools were used. Only medical records of adult patients, above 18 years old on ART were used, the variables included but were not limited to socio demographic data, viral load measurements, CD4 measurement, medical history records and anthropometric records.

3.2 Target Population

Adult patients on ART, above 18 years, who consented on their own, were enrolled into the study. These were patients seen at the Clinic during their routine clinic visit and suspected to be failing treatment and are either on first or second line treatment. Bomu Hospital has a total of 20788 adult patients registered at the hospital with 18 425 active on ART, while 2363 are still on care (Pre –ART). The number of total children on care are 1 863, of which 1 837 are on ART (Bomu Hospital medical records).

3.2.1 Study area

The study was conducted at Bomu Hospital. The hospital is a nonprofit, registered and recognized Non-Governmental healthcare organization that provides general medical, pediatric, antenatal, family planning, and HIV testing and care services established through PEPfAR funding. Bomu Hospital is in Mombasa County, Mombasa West in

Changamwe Sub County. It is located at 52^0 North East Changamwe at latitude $4^0$1'38''S 39^0 37'3"E.

3.3 Sample and Sampling Technique

Adults on first or second line antiretroviral treatment, 18 years and above, suspected of failing treatment, willing to consent on their own were included in the study. Men and women were given an equal chance to prevent bias of the data. However many women were enrolled in this study compared to men. Pregnant and breastfeeding women were not included in this study.

3.3.1 Sampling Technique

A convenient sampling technique was used in this study. This was to enable selection of cases that had the required information with respect to the objectives of the study. All patients on routine visits and those suspected with treatment failure and were on first or second line treatment was considered. However after viral load measurement is done, they were categorized into two groups. Those with viral load greater than or equal to 1000 copies per ml after more than one year on ART will be classified as failing treatment while those with less than 1000 copies per ml will be regarded as responding well to treatment.

3.3.2 Sample Size determination

The following formula (Daniel, 1999) given by equation 1 will be used:

$$n = \frac{Z^2 P(1-P)}{d^2} \qquad \text{Equation 3.1}$$

Where

n = sample size,

Z = Z statistic for a level of confidence (Reliability coefficient).

P = expected prevalence or proportion (In proportion of one; if %, P = 0.05), and

d = precision (In proportion of one; if 5%, d = 0.05).

Z statistic (Z):

For the level of confidence of 95%, was conventional used, *Z* value was 1.96. In this study, the results had 95% confidence intervals (CI).

Kenyan HIV prevalence was reported at 5.6% by 2012.Treatment failure rate documented at 5% (Bomu Hospital Medical Records, October 2014). The *d*- precision as half *P*. *d* in this case was 0.025.In this study 292 patients were recruited. 7 more patients voluntarily requested to join the study making a total of 299 patients.

3.3.3 Inclusion criteria

The criterion for selection of study participants was based on following considerations

1) Adult patients on ART for more than one year
2) Adult patients above 18 years of age
3) Patients suspected of failing either first or second line treatment

3.3.4 Exclusion criteria

1) The following categories of patients were excluded from the study.
2) New patients were not enrolled.
3) Patients on ART less than one year
4) Patients aged less than eighteen years. This was due to the inability to appropriately consent.
5) All patients who were pregnant

6) Patients who for personal reasons declined to participate in the study.

3.4 Research Instruments

A questionnaire was used to obtain the demographic and socioeconomic activities as given in appendix 2. A review of medical records was used to analyze the link between ARV treatment failures by looking at history of the participant that might have had an effect on ART. The selection of these tools was guided by the study objectives. The instruments were semi structured to enable a balance between quantity and quality of the data collected.

A 10ml volume of venous blood sample was collected on the day of enrollment from each patient and divided into three parts: one tested for absolute CD4+ T cell count at the laboratory using Becton Dickinson (BD) FacsCalibur flow Cytometer, and Full blood count. The other sample was sent to Bomu Hospital Laboratory for Viral load testing using Cavidi Exavir Load. The third part was tested for the liver and kidney function at the hospital laboratory as part of their routine testing and clinic health follow up.

3.5 Data Collection Procedures

Bomu Hospital approved the research to be conducted at the hospital. In addition informed consent was obtained from the study participants. Both quantitative and qualitative data was collected. The data was collected by qualified Clinicians and laboratory technologists with the help and supervision of the researcher so as to facilitate faster and more accurate data collection.

3.6 Pilot test

The interview schedule was pretested at Bomu Medical Centre –Likoni Branch on five patients on ART but was not included in the study sample, to assess the suitability of the questions during the enrollment process of the study participants. This was to enable the researcher to assess the validity and data reliability. The interview schedule was repeated with the same five patients after two weeks by a different interviewer to test for the reliability of the instrument and consistency of responses.

The pre-testing sought to find out the duration of the interview thus reduce the cost of hiring an additional staff. Irrelevant questions, correct language was taken into consideration. The interview aimed at standardizing the interview by different interviewers to minimize bias.

3.7 Data Processing and analysis

Data was analyzed using the Statistical Program for Social Scientist (SPSS) version 20 as an appropriate statistical tool for the largely descriptive nature of the study. Fisher's exact tests and unpaired t-tests was performed to compare clinical and laboratory characteristics according to viral load screening status. Multiple logistic regression attempts was used to determine the factors which could predict treatment failure and hence useful models for prediction of treatment failure could be used for decision making. A logistic regression model was given by equation 3.2.

$$y = \frac{e^{0.212x_1 + 0.011x_2}}{1 + e^{0.212x_1 + 0.011x_2}} \quad \text{. Equation 3.2.}$$

3.8 Ethical considerations

To ensure the protection of study participants, informed consent was obtained from all participants. Privacy and confidentiality was ensured by using study identity numbers.

All collected information was handled and stored with limited access. Findings of the study were to be communicated back to the participants and the facility. This study sought approval by Bomu Hospital and Jomo Kenyatta University College of Agriculture and Technology then sought ethical clearance at Pwani University Ethical Review Committee on behalf National Council for Science and Technology – NACOSTI, (Appendix 5).

CHAPTER FOUR

RESULTS

4.1 Socioeconomic and sociodemographic patterns

In this study a onetime viral load of greater than or equal to 1000 copies/ml was used to indicate treatment failure after a minimum period of one year of antiretroviral therapy. Study participants who failed to suppress the virus below 1000 copies /ml were classified non-suppressed and had treatment failure. Study participants with greater than 1000 copies/ml were classified as suppressed.

4.1.1 Viral suppression and gender

Out of the total number of 299 patients, 69 (23.1%) were not virally suppressed while 230(76.9%) had a viral suppression. This was further categorized as 151(76.3 %) and 47(23.7%) female suppressed and non-suppressed respectively. Among males 22(21.8%) did not suppress the virus while 79(78.2%) a good viral suppression. There was no association between gender and complete viral suppression whereas each had an equal chance, p value 0.144 and odd ratio of 1.118. This is summarized by table 4.1.

Note: Viral load $\geq$ 1000 copies/ml = Non Suppressed, while 0- 999 copies/ml = Suppressed.

Table 4.1: Viral suppression among males and females.

	Viral Response						
Sex	Non Suppressed	Suppressed	Total	Pearson Chi-Square	df	P value	Odd ratio
	47(23.7%)	151(76.3%)	198				
Female							
Male	22(21.8)	79(78.2%)	101				
Total	69(23.1%)	230(76.9%)	299	0.144	1	0.704	1.118

4.1.2 Viral suppression and herbal usage

It was seen that some patients used herbal treatments together with the ARVs either for their opportunistic infections or as a result of claims by herbalists to provide complete cure of HIV/AIDS. Different types of herbal medications were used by the study participants. These herbal drugs were indigenous and were generally classified as herbal drugs. The use of herbal drugs together with the ARVs had no association, 23(67.6%) using herbal drugs and 207(78.1%) not using herbal drugs had a complete viral suppression, p value 0.173. The results are summarized as shown in table 4.2 below.

Table 4.2: Viral suppression and the use of herbal drugs together with ARVs

Viral Response							
Use of Herbal drugs	**Viral response**		**Total**	Pearson Chi-Square	df	P value	Odd ratio
	Non Suppressed	Suppressed					
No	58(21.9%)	207(78.1%)	265	1.859	1	0.173	0.586
` Yes	11(32.4%)	23(67.6%)	34				
Total	69(23.1%)	230(76.9%)	299				

4.1.3 Viral suppression and alcohol consumption

11(73.3%) had a complete viral suppression among those on alcohol use while 4 (26.7%) failed to achieve viral suppression. There was no association between viral suppression and alcohol consumption, p value 0.735. The results are shown in table 4.3.

Table 4.3: Use of alcohol and viral suppression.

Viral response							
Alcohol use	Viral response		Total	Pearson Chi-Square	df	P value	Odd ratio
	Non Suppressed	Suppressed					
No	65(22.9%)	219(77.1%)	284	0.115	1	0.735	0.816
Yes	4(26.7%)	11(73.3%)	15				
Total	69(23.1%)	230(76.9%)	299				

4.1.4 Viral suppression among age groups

Patients above 18 years of age who met the inclusion criteria were recruited in the study. The age groups were categorized as per table 4.4. A good viral suppression was seen among the elderly population. The age groups 41-50 and 51-60 had a good viral suppression of 80.7% and 88.2% respectively.

Table 4.4: Viral suppression among age groups

	Viral response					
Age groups in Years	Non Suppressed	Suppressed	Total	Pearson Chi-Square	Df	P value
Less than 20	1(50%)	1(50%)	2			
21-30	14(36.8%)	24(63.2%)	38			
31-40	25(24,5%	77(75.5%)	102			
41-50	27(19.3%)	113(80.5%)	140	7.350	4	0.119
51-60	2(11.8%)	15(88.2%)	17			
Total	69(23.1%)	230(76.9%)	299			

4.1.5 Viral suppression and marital status

Study participants were classified as divorced, married, widowed or still single. Using Chi square test of independence (Fisher exact test) it was found that there are significant associations at 5% level of significance between viral suppression and some of the sociodemographic factors namely marital status and age groups. The elderly tended to respond more compared to the young and the married people tend to respond more compared to other segment of marital status. Table 4.5 summarizes the viral suppression responses among these different classes.

Table 4.5: Viral suppression and marital status

Marital status	Viral response		Total	Pearson Chi-Square	df	P value
	Non Suppressed	Suppressed				
Divorced	16(40%)	24(60%)	40			
Married	31(18.7%)	135(81.3%)	166			
Single	15(34.9%)	28(65.1%)	43	13.963	3	0.003
Widowed	7(14%)	43(86%)	50			
Total	69(23.1%)	230(76.9%)	299			

4.1.6 Viral suppression and occupation

On employment status it was seen that majority of the study participants were self-employed. One student was enrolled in the study with a 100% poor viral response. Both the employed 75(78.1%) and unemployed 76(79.2%) had a complete viral suppression. There is no association between viral suppression and employment levels, p value 0.259. Table 4.6 summarizes viral suppression and occupation.

Table 4.6: Viral Suppression and employment levels

Occupation	Viral response		Total	Pearson Chi-Square	df	P value
	Non Suppressed	Suppressed				
Employed	21(21.9%)	75(78.1)	96			
Self Employed	27(25.5)	79(74.5%)	106			
Student	1(100%)	0(0%)	1	4.026	3	0.259
Unemployed	20(20.8%)	76(79.2%)	96			
Total	69(20.8%)	230(79.2%)	299			

4.1.7 Viral suppression and smoking

The results show that 10 study participants were smokers in their course of antiretroviral treatment. 4 (40%) of them had a poor viral suppression while 6(60%) had a complete viral suppression. 289 study participants were non-smokers, 65(22.5%) had no viral suppression while 224(77.5%) had a complete viral suppression. These results show no association between viral suppression and smoking, p value 0.196. Either a smoker or a non-smoker had an equal chance of incomplete viral suppression, odds ratio 0.435. This is summarized in table 4.7 below.

Table 4.7: Viral suppression and smoking

Smoking	**Viral response**		Total	Pearson Chi-Square	Df	P value	Odd ratio
	Non Suppressed	Suppressed					
No	65(22.5%)	224(77.5%)	289	1.669	1	0.196	0.435
Yes	4(40.0)	6(60.0%)	10				
Total	69(23.1%)	230(76.9%)	299				

4.1.8 Viral suppression and salary

The level of income earning has a direct impact of the economic wellbeing of any individual. The results show that the economic wellbeing as well as a complete viral suppression was realized among the study participants with higher earnings. Study participants with salaries over Ksh 40,000 had 100% viral suppression. Table 4.8 summarizes the findings.

Table 4.8: Viral suppression and salary

Salary in Ksh	Non Suppressed	Suppressed	Total	Chi square	P value
Less than 10,000	31(26.3%)	87(73.7%)	118		
10,001 – 20,000	7(17.5%)	33(82.5%)	40		
20,001 - 30,000	4(20.0%)	16(80.0%)	20		
30,001 - 40,000	4(50.0%)	4(50.0%)	8	6.303	.278
40,000 – 50, 000	0(0%)	4(100%)	4		
50,000 – 60,000	0(0%)	2(100%)	2		
Total	**46 (23.1%)**	**146(76.0%)**	**192**		

4.1.9 Multiple logistic Regression

Using the logistic regression can be fit as

$$y = \frac{e^{0.212x_1+0.011x_2}}{1+e^{0.212x_1+0.011x_2}} \qquad \text{Equation 4.1}$$

Where x_1 is the age group and x_2 is the marital status. Using the above model the probability of a patient responding can be estimated given their age group and marital status keeping other factors constant.

4.2 Relationship between the duration of treatment and treatment failure

The number of years on antiretroviral use has no effect on treatment failure. It was seen that there was no relationship on the duration of ARV use and treatment failure. This is shown in table 4.9.

Table 4.9: Correlation between years on ARV use and viral suppression

Years on ART	Viral response		Total	Pearson Chi-Square	Df	P value
	Non Suppressed	Suppressed				
1-4	20(22%)	73(78%)	93			
5-8	39(30%)	93(70%)	132			
9-12	10(14%)	59(86%)	69	7.605	3	0.055
13-16	0(0%)	5(100%)	5			
Total	69(23%)	230(77%)	299			

4.3 Co infections and antiretroviral treatment

There was no association between viral suppression among the study participants with or without co infections in there course of ARVs treatment, chi square 0.145, p value 0.703. Study participants had an equal chance of getting co infection even with complete viral suppression, odds ratio of 1.111 as shown in Table 4.10.

Table 4:10: Co infections and viral suppression

	Co infections						
Co infections	Non Suppressed	Suppressed	Total	Pearson Chi-Square	df	P value	Odd ratio
No	33(24%)	104(76%)	137	0.145	1	0.703	1.111
Yes	36(22%)	12678%)	162				
Total	69(23%)	230(77%)	299				

4.4 Relationship between treatment failure and CD4 cell count

A correlation between viral suppression and CD4 is significant at p value 0.000 level. There is positive significant relationship between the viral suppression and current CD4 cell count. The viral suppression is higher among those with high CD4 cell counts .This is given by table 4.11

Table 4.11: Association between viral response and CD4

	Viral response					
CD4 Range(cells/µL)	Non Suppressed	Suppressed	Total	Pearson Chi-Square	df	P value
0-500	60(35%)	110(65%)	170			
501-1000	9(8%)	101(92%)	110			
1001-1500	0(0%)	15(100%)	15	33.742	4	0.000
1501-2000	0(0%)	3(100%)	3			
2501-3000	0(0%)	1(100%)				
Total	69(23%)	230(77%)	299			

Using independent t test it can be shown that there was significant difference in means in CD4 cells between the two groups; the responsive and non-responsive. Table 4.13 presents these results.

CHAPTER FIVE

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Differences in gender.

At Bomu Hospital, gender was not found to be a predictor of either complete or incomplete viral suppression as there was no difference among male and female patients. This is contrary to a similar study which showed that men on ART were more vulnerable to virologic failure than women (Gebo *et al*., 2005).

Out of the total number of 299 patients, 198 (66%) were females and 101 (34%) 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 register as reported by Mugusi *et al.*, 2010. 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 (Mugusi *et al*., 2010).

Female patients were more on HAART compared to male; though this was not conclusive that female had a higher prevalence compared to men. Gender related treatment failure results had no difference among males and females may be due to socio cultural and anatomical measures among others which lead to this unfortunate trend. The conclusion was that in most Sub Saharan African countries, proportionally more females are on HIV antiretroviral treatment than men.

5.1.2 Use of herbal medicine

Traditional medicines are an integral part of health care worldwide, even though their efficacy has not been scientifically proven (Gwaza *et al*., 2013). The use of traditional medicines with antiretroviral drugs (ARVs) has created a problem because drug interactions compromise the efficacy of ARVs (Gwaza *et al.*, 2013). However, there are still ethical issues regarding traditional medicines that need to be addressed, for example, regulations regarding quality control and standardization of medicines, regulation and education of healers who deliver these medicines and unregulated clinical trials.

In this study the herbal drugs were generally indigenous hence could not be classified. There was no difference in viral suppression among these two groups. The number of study participants on herbal medicine was small hence could not give conclusive evidence. Similar studies statistically found that in general, the effect of concomitant ARV and herbal use was not clinically significant. This was in concordance with a Gwaza *et al.*, 2013 study on adult volunteers which showed that hypoxis is not associated with clinically significant changes in the pharmacokinetics of the ARV agent, LPV/r pharmacokinetics.

5.1.3 Use of alcohol and smoking

Tobacco smoking common in people living with HIV is associated with increased mortality and morbidity (Bhatta, Subedi and Sharma, 2018).Smoking and alcohol consumption alters immune and virological responses leading to increased vulnerability to infection, tuberculosis and low adherence to ART (Bhatta, Subedi and Sharma, 2018). Alcohol consumption often overlaps with other health conditions or behaviors that could be linked to poor HIV viral suppression, including social aspects such as homelessness, depression and other substance use (Cook *et al*., 2017).

The number of study participants either smoking or on alcohol consumption was small hence could not give conclusive evidence. However patients visiting health facilities must be routinely screened for alcohol and substance abuse to ensure strict adherence. Alcohol abuse and smoking is associated with increased morbidity and mortality (Lifson *et al.*, 2010). Pertinent knowledge regarding patient alcohol consumption while taking ARV needs to be disseminated to all primary healthcare workers as this has a direct impact on patient adherence levels.

5.1.4 Age and viral suppression

A good viral suppression was seen among the elderly group compared to the young generation. In this study the age brackets 31- 40years, 41 – 50 years, 51 – 60 years, had a viral suppression of 75.5%, 80.7 % and 88.2% respectively.

Younger age has been associated with lower rates of virologic suppression in prior studies (Mujugira *et al.,* 2016). A study of approximately 9000 adults on ART in south Africa found lower rates of virologic suppression in younger adults (16 - 24years) compared with those aged 25 -49 years (Mujugira *et al*., 2016).

Gutierrez *et al*., 2007 findings showed that the elderly at initiation of HAART predicts an unfavorable outcome in patients and other studies have shown that younger age appears to be associated with a good immunological response. (Viard *et al*., 2001) and older age has often been associated with a blunted CD4 response despite suppression of viral replication (Schechter, 2006).

These data suggest that younger age predicts failure to achieve viral suppression and the risk decreases with age. The elderly may be adherent and more sensitive than younger people. This might be attributed to the fact that older people tend to be more responsible with their health. However, the data was skewed towards older people, which may also have impacted the results.

5.1.5 Marital status

In this study the married people had a good viral suppression compared to the other segment of marital status. Spousal support plays an important role in improving any form of treatment (Kayeyi, Fylkesnes, Michelo, Makasa, and Sandoy, 2012). Psychologically married patients have easier access to assistance from their family higher levels of fighting spirit and lower levers of distress (McMahon, Wanke, Terrin, Skinner, and Knox, 2010).

5.1.6 HIV treatment outcomes on employment and income levels

Socioeconomic position is an aggregate of resources including education, employment, income and wealth that interact but are not interchangeable, and is linked to health outcomes in a variety of diseases and setting (Flynn *et al*., 2017). Among HIV-infected individuals receiving antiretroviral therapy (ART) in high-income countries, less wealth, income or formal education conveys risk for poorer survival (McMahon, Wanke, Terin, Skinner, and Knox, 2010). Existing literature widely encourages socioeconomic interventions for HIV patients receiving ART to promote successful long-term disease control (Tulisuna -Alama *et al.,* 2012).

Majority of patients attending Bomu Hospital are low and middle income earners with income less than Ksh 30,000 per month. The study findings showed no relationship in viral response based on income and employment levels.

5.1.7 Duration of antiretroviral treatment and viral suppression.

Studies agreed that most of the treatment failure occur during the early days of ART initiation (Kantor *et al*., 2009). In this study the years on antiretroviral use and viral suppression was not significant. The duration of antiretroviral treatment had not negative outcome. Treatment failure often occurs during the first early months of therapy due to

poor adherence, poor status disclosure, severe drug toxicity and regimen changes (Kantor *et al*., 2009).

5.1.8 Opportunistic infections in HIV treatment outcomes

TB co infection is one of the most consistent predictor of treatment failure among ART patients (Bansi *et a*l., 2010). Based on the sample selected on this study, there was no relationship between viral suppression and co infections. Other studies reported that not only TB co infection, but also developing TB is associated with treatment failure, and also having other opportunistic infections is significantly associated with treatment failure (Ledergerber, 2004).

5.1.9 Relationship between viral response and CD4 cell count

A good viral suppression was seen among those with high CD4+ cell counts. These data suggest relationship exists for immune reconstitution and suppression of plasma viral load. A similar study indicates that virological suppression ensures the recovery of CD4 cells levels that reduces the risk of opportunistic infections and increase life expectancy (Finzi *et al*., 1999). The result of this study demonstrates that HIV suppression restores HIV specific CD4 (+) T cell multifunctional immunity and balance.

5.2 Conclusions

The average viral suppression in this cohort was 76.9% against the national target of 90% (NASCOP, 2019). Patients above 41 years had a good viral suppression compared the patients less than 41 years. Bomu Hospital and all national projects involved in HIV care and treatment should target the youth less than 19 years and young adults 20 – 40 years to increase the national viral suppression target of 90% and above. Not all patients with opportunistic infections had treatment failure. There was no significant difference in treatment outcome among male and female, herbal medicine, alcohol use and

smoking, however the sample size was small. There exists a relationship between immune reconstitution and suppression of plasma viral load.

5.3 Recommendations

5.3.1 Application of the findings

1) The viral suppression for Bomu Hospital was 76.9% was lower compared to the national target of 90%. Mechanisms should be put in place to identify patients with high viral load at high risk of treatment failure early. High risk patients should be flagged for closer monitoring.
2) Bomu Hospital and all national projects at large involved in HIV care and treatment should target the youth and middle aged patients to increase the national viral suppression target.
3) Opportunistic infections should be treated on isolation as they don't warrant ARV treatment failure or change in ART regimen.
4) A further study on herbal medicine use together with ARVs, classification of the herbal drugs is recommended.

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APPENDICES

Appendix I: Participants' Consent Statement

Hello, my name is Mussa Mwamzuka. I am carrying out a research into the Factors Influencing Antiretroviral treatment Failure among adults HIV patients on treatment at Bomu Hospital as part of my thesis towards the award of Msc. Degree in Public Health of Jomo Kenyatta University of Agriculture and Technology. 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 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_____

Appendix II: Questionnaire

STUDY ID ……..

A. Demographic data

1) Age: …….. Cohort …… Residence……

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) Specify……..

B. Socioeconomic status

1) What is your highest level of education?

a) Primary b) Secondary c) Mid-level college d) University f) No response

2) What is your average monthly income? Ksh……

3) What is your occupation?

(a) Student (b) Unemployed (c) Paid employee (d) self employed

C. Infection history (Infection awareness history)

1) For how long have you known you are infected with HIV? ……..…… Years
2) How did you become aware of your HIV status?

(a) Diagnostic- DTC (b) VCT (c) PMTCT (d) TB Clinic (e) PITC (f) Admitted

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

(a) Contaminated instruments (b) blood donation (c) heterosexual contact (d) homosexual contact (e) witchcraft (f) cannot tell

Treatment history.

4) Before you were diagnosed HIV positive and not on ARVs did you receive treatment for some conditions that suggested to you that you w☐ill? ☐

Yes No

What kind of illness was it? …….....**.....**

5) Have you suffered any other ailment while on ARVs Yes ☐ No ☐

If Yes, what kind of disease (ailment)……..

6) Did you receive treatment for this ailment? Yes ☐ No☐

7) Have you suffered from TB Yes ☐ No☐

If Yes, when was it? ☐ Before being on ARVs ☐ While on ARVs

D. ARV Treatment at Bomu Hospital

1) Do you receive antiretroviral medicines Bomu? Yes ☐ No ☐

2) How many HIV/AIDS medications do you take at a time?

One ☐ Two ☐ Three ☐ Others ☐

3) What's the frequency of medication?

(a) Once daily (b) Twice daily (c) three times daily (d) others…….

4) Do you receive regular supplies of antiretroviral medicines? ☐ ☐

No

5) Were there times that you did not receive ARV drug supplies? Y☐ ☐

No

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

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

7) Were there times you could not afford to come for ARVs due to lack of resources?

Yes ☐ No ☐

F. Other Drug combinations

8) Have you mixed ARV with herbal medication? 1 – Yes 2- No
If Yes name the herbal drug ……..

9) How long have you used the herbal drug? ……...

10) Are you still using the herbal drug? 1 = Yes 2 = No

11) Have you used other drugs while on ARVs? 1 = Yes 2 = No

If YES, which drugs did you use

……

……

…….

How long did you use these drugs? .....

12) In the Past 3 months, have you smoked cigarettes? 1 = Yes 2 = No

13) Any History of alcohol use in the past 3 months 1 = Yes 2 = No

If Yes, how frequent 1=Daily 2= Weekly 3 = can't remember

G. Assessing adherence to therapy at Bomu

1) For how long have you been on treatment at on ARVs_____

2) Have you had ARV treatment interruption before? Yes ☐ No ☐

3) If yes,

How often did it happen? (a) Once (b) twice (c) three times (d) Others.……

4) What was the duration of treatment interruption?

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

5) What made you interrupt your treatment?

(a) Illness (b) distance (c) financial (d) Pill burden (e) Other…… ……

6) Is there anything that makes it difficult for you to take your medicines?

Yes ☐ No. ☐

If yes, what is it?

(a) Pill burden (b) side effects (c) dosage frequency (d) other……..

7) Now I would like you to make some comments regarding your treatment at Bomu

   Hospital._____

8) Location of the clinic promotes confidentiality. True ☐ False ☐

9) Services rendered by:

   i) Counselors,

      (a) Appreciable (b) not appreciable (c) other……..

   ii) Nursing staff,

      (a) Appreciable (b) not appreciable (c) other……..

   iii) Doctors,

      (a) Appreciable (b) not appreciable (c) other……..

   iv) Pharmacy staff,

      (a) Appreciable (b) not appreciable (c) other……

   v) Laboratory staff,

      (a) Appreciable (b) not appreciable (c) other…

Appendix III: Clinical Data Tool

CHWE Number _____Bill Number_____STUDY ID_____

A	DEMOGRAPHICS		
	Age		
	Gender	Male	Female
B	IMMUNOLOGICAL STATUS		
	Current CD4	CD4 6 month ago	CD4 12 months ago
C	HISTORY OF VIRAL LOADS		
	Current Viral load	Previous Viral load	Others
D	ARV TREATMENT HISTORY		
	ARV used before starting HAART		
	Current Regimen		
	Drugs substituted		
	Drug Adjustment		
	Other Drugs used together with ARVS		
E	LAB RESULTS		

	HB	
	ALT(GPT)	
	AST(GOT)	
	Serum Creatinine	
	Others	
	1.Hepatitis B	
	2 Hepatitis C	
F	WHO STAGING	
	Current Stage	
	Staging (6 months Back)	
	Staging (12 Months Back)	
G	ADHERENCE COUNSELLING (Good, Fair, Poor)	
	Current	
	6 months Back	
	12 months	
H	HISTORY OPPORTUNISTIC INFECTIONS	
	1	2
	3	4

Appendix 1V: Clearance Letter from Bomu Hospital

BOMU HOSPITAL
Health Hope Humanity

MCS/ADMIN/0550/2016

20th January 2016

To

Mussa Mwamzuka

Bomu Hospital

P.O.Box 95683-80106

Mombasa .

Dear Mr. Mussa,

REF: FACTORS INFLUENCING ANTIRETROVIRAL TREATMENT FAILURE AMONG ADULT HIV PATIENTS ON TREATMENT AT BOMU HOSPITAL

Reference is made to your application dated 15th January 2016 requesting permission to conduct the above mentioned study at this hospital. The proposal has been evaluated and found to have merit. Kindly be informed that the approval has been granted under the following conditions:

1. Informed consent shall be sought and obtained from all patients before interview and sample collection is conducted.
2. Confidentiality of patient data will be ensured as stated in the research proposal.

You are also requested to share the findings of your study with the relevant hospital department when you complete your thesis.

I wish you success in your undertaking.

Sincerely,

BOMU HOSPITAL
A PROJECT OF MUSLIM CLINIC SOCIETY
P.O. Box 95683 - 80106
Tel: +254 20 2331444 2652555
+254 4755

Dr. Aabid Ahmed M.B.Ch.B., MSc. CRA (UK),
Chief Executive Officer,
Bomu Hospital.

P.O. Box 95683 – 80101, Mombasa, Kenya
Tel: +254 20 233 1444 / 235 2555
Email: info@bomuhospital.org
www.bomuhospital.org

Appendix V: Certificate of Ethical Approval

Pwani UNIVERSITY

ETHICS REVIEW COMMITTEE

ACCREDITTED BY THE NATIONAL COMMISSION FOR SCIENCE, TECHNOLOGY AND INNOVATION (NACOSTI, KENYA)

CERTIFICATE OF ETHICAL APPROVAL

THIS IS TO CERTIFY THAT THE PROPOSAL SUBMITTED BY:

MUSA MWAMZUKA

REFERENCE NO:
ERC/MSc/042/2016

ENTITLED:
Factors influencing antiretroviral treatment failure among adult HIV patients on treatment at Bomu Hospital

TO BE UNDERTAKEN AT:
MOMBASA COUNTY

FOR THE PROPOSED PERIOD OF RESEARCH

HAS BEEN **APPROVED** BY THE ETHICS REVIEW COMMITTEE

AT ITS SITTING HELD AT PWANI UNIVERSITY, KENYA

ON THE 21ST **DAY OF MARCH 2016**

CHAIRMAN SECRETARY LAY MEMBER

PTO

Pwani UNIVERSITY

Ethics Review Committee,
Pwani University, www.pu.ac.ke, email: t.rewe@pu.ac.ke, tell: 0719 182218.
The ERC, Giving Integrity to Research for Sustainable Development

NOTICE:

This decision is subject to the information available at the time of APPROVAL. The Committee may on its own motion and/or by application by a Party, review its decision on the grounds of discovery of new and important information which was not reasonably within its knowledge at the time of decision or on account of mistake or error apparent on the face of the record, or for any other sufficient reason, provided the researcher shall be given prior opportunity to be heard.