FACTORS LEADING TO ELEVATED VIRAL LOAD AMONG HIV INFECTED INDIVIDUALS RECEIVING ANTIRETROVIRAL THERAPY IN PWANI REGION, TANZANIA

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By

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A dissertation Submitted in (partial) Fulfillment of the Requirement for the Degree of Master of Science (Epidemiology and Laboratory Management) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Factors leading to elevated viral load among HIV infected individuals receiving antiretroviral therapy in Pwani region, Tanzania,*** in (Partial) fulfillment of the requirement for the degree of Master of Science (Epidemiology and Laboratory Management) of the Muhimbili University of Health and Allied Sciences.

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DECLARATION

AND

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I, **Josiah Isaac Mutigitu** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for similar or any other degree award.

Signature…… Date……

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DEDICATION

This dissertation is dedicated to my lovely family for their love and patience over the whole period when I was not at home. In such away my family missed my love and care as a father. Furthermore, I dedicate this work to Dr. Abade and Dr. Fausta for their love, care and courage. Sometimes I felt so exhausted in the journey but they continuously encouraged me, which gave me strength to move ahead.

ABSTRACT

Background

Antiretroviral therapy (ART) has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition. The quantification of viral load in plasma is a determinant of the progression of the disease and, along with CD4 lymphocyte counts, has been used to monitor therapeutic responses in HIV patients on ART.

Objective

To determine the factors leading to elevated viral load among HIV infected individuals receiving ART in Pwani region Tanzania.

Methodology

This study was analytical cross sectional facility based among a cohort of Patient attending three hospitals in Pwani Region. The study was conducted for a period of 12 months using viral load data collected at care and treatment clinic (CTC) in Pwani region from June 2016 to May 2017. A total of 482 HIV infected individuals enrolled on ART in Pwani region were included in this study. Plasma viral load results were obtained from patient's medical record files. Structured questionnaires were administered to participants to gather information on factors associated with elevation of viral load. Viral load was also tested after 12 months or more of using ART i.e. six months from the initial viral load test. Data analysis was done using Epi info version 3.5.1. Chi squared-Mantel-Hansel test was used to for comparison of proportions. Logistic regression and multivariate analysis were used to analyze factors associated with elevated viral load.

Results

A total of 482 HIV infected individuals were recruited in the study. The proportion of participants with elevated viral load (>1000 copies/mL) was 188 (39%). The median viral load results obtained in patients' medical records after period of six months or more of using ART was 12368 copies/mL (IQR=3999-47236) which decreased significantly to 437 copies/mL (IQR=20-9303) after being on enhanced adherence counseling and close follow

up by health worker. In this study, we found the following factors were significantly associated with elevated viral load; HIV infected individuals who had not disclosed their HIV status were four times more likely to have elevated viral load compared to those who disclosed their HIV status (OR=3.78 95% CI (1.78-7.88). HIV infected individuals who did not attend enhanced adherence counseling were three times more likely to have elevated viral load compared to those who attended (OR= 3.08 95% CI (1.74- 5.46). Those who reported to be taking alcohol were three times more likely to have elevated viral load compared to those who reported not to be taking alcohol (OR=3.49 95% CI (2.09 – 5.82). Moreover, individuals who were not members of psychosocial groups were three times more likely to have elevated viral load compared to those who were members of psychosocial groups (OR=2.64 95% CI (1.28-5.44). Participants who reported to take two meals or less per day were two times likely to have elevated viral load compared to those who reported to take more than two meals per day (OR= 1.64 95% CI (1.13-2.38). HIV infected individuals who could not take medication on an empty stomach were four times more likely to have elevated viral load compared to those who were able to take medication even on empty stomach (OR= 4.03 95% CI (2.47- 5.98),

Conclusion

While ART has made it possible to significantly decrease of HIV related morbidity and mortality, this study found a high proportion (39.%) of individual had elevated viral load despite being on ART for 12 months or more. The factors which influence the elevation of viral load in patients using ART in Pwani region, included taking alcohol, taking few meals per day, not attending EAC session, failing to take medication in empty stomach, consuming few number of meals per day, not being member of psychosocial group and failing to disclose their HIV status. This study also found that being depressed or having illness, forgetting or being busy, unavailability of ART at the clinic, change of daily routine were among the reasons for non-adherence to ART.

Recommendation

Emphasis should be made by health-care providers to enhance adherence and counseling to all HIV infected patients at the time of ART initiation. Patients should also be encouraged by health care providers to join a psychosocial group where they will receive psychosocial

support to help them to cope with fear of disclosing their HIV status as well as stigma. We also recommend for another study to assess the role of antiretroviral drug resistance on persistence of high level HIV viral load, particularly for patients with elevated viral load after 12 months of ART despite being on enhanced adherence and counseling groups.

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DEFINITION OF TERMS

Viral load is the term used to describe the amount of HIV in blood. **Viral load** tests measure the amount of HIV's genetic material in a blood sample. The results of a **viral load** test are described as the number of copies of HIV RNA in a millilitre of blood. When results are ≥ 1000copies per millitre it terms as **elevated viral load.**

ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
CHWs	Community Health Workers
CTC	Care and Treatment Centers
DNA	Deoxyribonucleic Acid
EAC	Enhanced adherence counseling
HF	Health Facility
HIV	Human Immunodeficiency Virus
MOHCDGEC	Ministry of Health Community Development Gender Elderly and Children
NACP	National AIDS Control Program
NHLQATC	National Health Laboratory Quality Assurance and Training Centre
NNRTIs	Non-nucleoside reverses transcriptase inhibitors
PCR	Polymerase Chain Reaction
PI	Protease inhibitor
PITC	Provider Initiated Testing and Counseling
RNA	Ribonucleic Acid
VL	Viral load
WHO	World Health Organization

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND

Antiretroviral therapy (ART) for the treatment of Human immunodeficiency (HIV) infection has improved steadily since the advent of potent combination therapy (1). With advancement in treatment for HIV, there has been significant improvement in the safety and tolerability of ART regimens. ART has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition (2). The pill burden and dosing frequency for Antiretroviral (ARVs) have been reduced and adverse events minimized; all of which have contributed to the success rates in initial treatment (1)**.**

In addition, treatment of HIV-infected individuals with ART is highly effective at preventing transmission to sexual partners. The currently existing and commercially available antiretroviral drugs in Tanzania includes Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) and Protease Inhibitors (PIs) (3–6).

ART has improved the survival and quality of life of patients with HIV/AIDS (2). Because it reduces viral load (7) and increases the CD4 T-cells which improves the immune system of the patient (6). The quantification of viral load in plasma is one of the determinant of disease progression (8), and along with CD4 lymphocyte counts, have been used to monitor therapeutic responses (3,6). Determinants of undetectable viral load in patients on ART are important, however viral load testing are relatively scarce in many care and treatment clinic (CTC) settings especially in resource limited countries (9)**.** The first four to six weeks of ART are marked by a trend of reduction in viremia of at least 1.0 log10, which represents 90% of the initial viremia and, in the next 12 to 24 weeks the viremia is expected to be undetectable or 99% lower than the initial level or from 5,000-10,000 copies/ml (6). Prevalence of undetectable viral load increases between three and six months of treatment, and that there is no evidence of changes in this prevalence after that period (6)**.** Reduction in viral load is greater during the first year of treatment (10).

The level of adherence to ART has been considered the most important predictor of viral load in patients receiving treatment. It is suggested that the viral load would decrease (11) and the prevalence of undetectable viral load would increase (12) as adherence increases and high adherence rates are usually necessary for attaining therapeutic effectiveness. A study conducted in Brazil showed that, the prevalence of undetectable viral load in 78% of the patients whose adherence rates were 95% or greater; the prevalence decreased to 39% in patients with adherence rates between 80% and 94% and to 20% in those whose adherence rate was less than 80% (12). There is a strong linear association between undetectable viral load and adherence; in patients with adherence higher than 97%, the prevalence of undetectable viral load was approximately 60% (13). Higher prevalence of undetectable viral load and lower levels of viral load were observed at the age above 45 (14), female sex (15), stable immune status (evidenced by CD4 counts higher than 200 cells/mm3) (15), and lower levels of viral load at the beginning of treatment (8,11,12).

According to national guidelines for the management of HIV and AIDS prepared by national AIDS control programme (NACP) in Tanzania, guiding principle for monitoring patient is that the availability of laboratory monitoring is not a prerequisite for the initiation of ART, viral load testing is essential for monitoring patients on ART. Viral load testing should be done six months after initiation of ART and then at least after every 12 months for patients with suppressed Viral Load (below 1000 cp/mL (1). In Tanzania, clinical assessment and laboratory tests play a key role in assessing individuals before ART is initiated and then monitoring their treatment response. A successful ART results is decrease of viral load, immune recovery and therefore increases in number of CD4 cells.A repeat HIV viral load test will be performed after three months of intensive adherence counseling if the preceding HIV viral load test result was more than 1000 cp/mL. An HIV viral load test will be performed annually if two preceding HIV viral load test results were less than 1000 copies/mL.

In the past years, CD4 cell counts were used to determine progress of HIV infected patients and also to determine the ART eligibility and initiation. Routine viral load monitoring in Tanzania started in June 2016. In Tanzania, viral load testing is performed in few facilities like 52 facilities (17 using COBAS AmpliPrep/COBAS TagMan HIV-1 Test v 2.0 and 35 using Gen X-part to zones Referral hospital and some of Regional referral hospitals and the

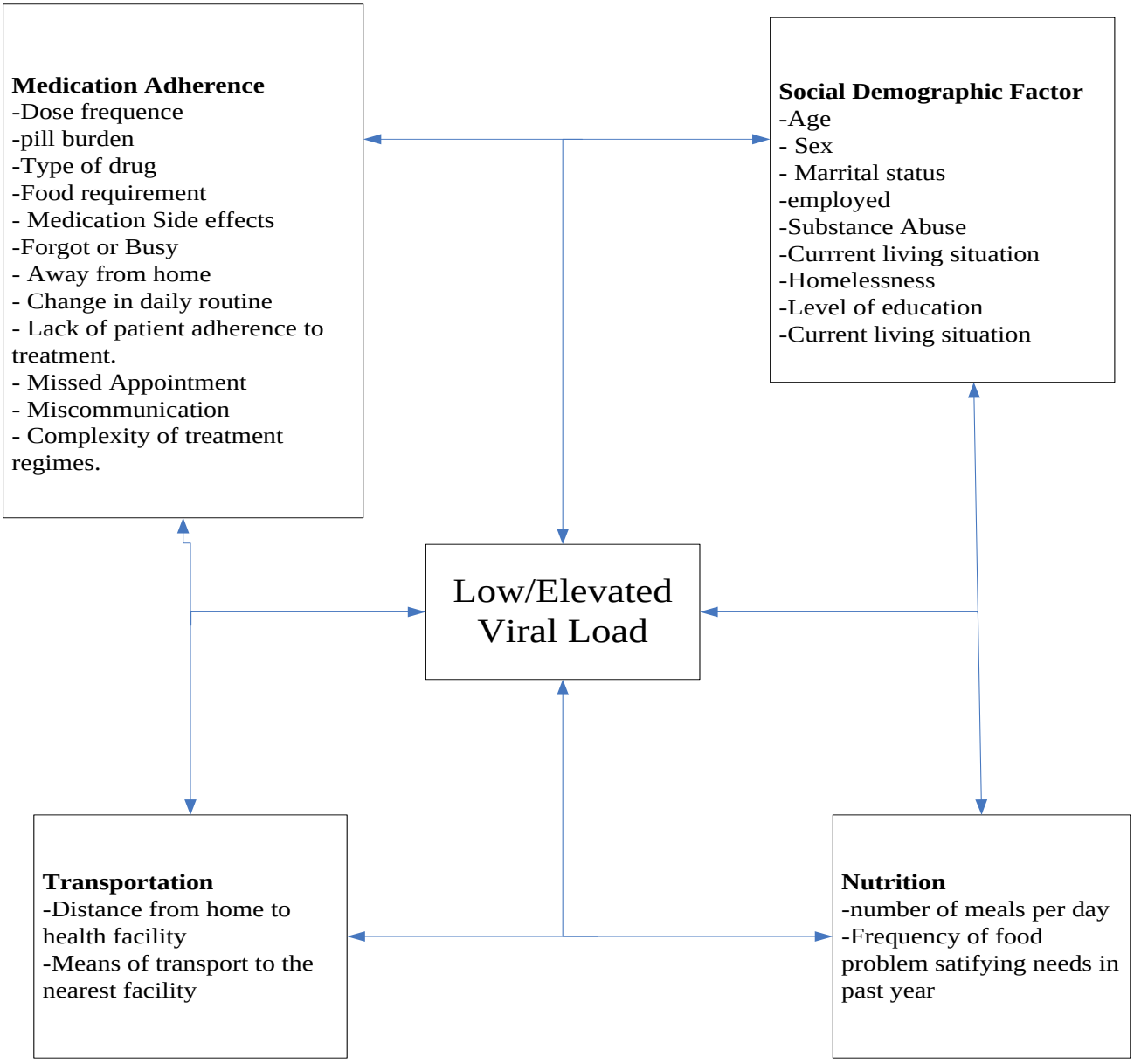
Ministry of Health Community Development Gender Elderly and Children (MOHCDGEC) is planning to scale up and making the service available country-wide (ie to regional and district hospital).

This study was conducted to determine the factors associated with elevated viral load among HIV-infected individuals receiving ART in Pwani region, Tanzania assuming that all started ART in previous years had elevated viral load above 1000 copies/mL.

1.2 Problem statement

HIV and AIDS prevention; care, treatment and support services, relies on laboratory testing where tests like CD4 cell count and viral load test are critical in providing information on an individual's HIV status, disease staging, and treatment eligibility as well as ART monitoring. Clinical assessment and laboratory tests play a key role in assessing individuals before ART initiation and then monitor the treatment response to ART. Viral load is a preferred monitoring approach for diagnosis and confirmation of ART failure or successfulness of ART, which result in decrease of viral load, immune recovery and therefore increases in number of CD4+ T cells. Review of unpublished report of June, 2016 to March, 2017 from National Health Laboratory Quality Assurance and Training Centre (NHQATC) on analysis of viral load data obtained from patients on ART showed that, there was an increase in viral load among patients who were on ART for six months or more. However, little was known about factors associated with the increase of viral load among HIV infected individuals receiving ART in Pwani region. Therefore, there was a need to understand factors that lead to the elevation of viral load among HIV infected individuals using ART.

1.3 Conceptual Framework



Source of conceptual framework:

This conceptual framework was constructed from different reports that were published previously (3–5,17).

1.4 Conceptual framework description.

The conceptual framework shows how various factors can interact and determine the level of viral load as a dependent variable. In this study, independent variables were (medication adherence, social demographic factors, nutritional factors and transportation have direct linkage with the dependent variables).

Some of the independent variable has interaction with each other such as social demographic factors i.e. age can interact with medication. Although adherence factors like type of drugs or pill burden and transportation factors like distance from home to health facility can have an interaction with medication adherence factors like dose frequency and missed appointment.

1.5 Rationale of the study

Tanzania through the MOHCDGEC has implemented viral load testing in various hospitals and health facilities in order to monitor ART response among HIV infected individuals. Data generated from this study will help to understand the factors contributing to the increase of viral load among HIV infected individuals that will help to improve public health activities/interventions towards the reduction of viral load in patients living with HIV/AIDS.

1.6 Research Question

1. What is the proportion of HIV infected individuals with high viral load after six months or more of ART initiation in Pwani region in Tanzania?
2. What are the factors associated with elevation of viral load among HIV infected individuals after being on ART for six months or more?

1.7 Broad Objectives

To determine factors leading to elevated viral load among HIV infected individuals receiving ART in Pwani region Tanzania.

1.8 Specific objectives

1. To determine the proportion of HIV infected individuals with high viral load after six months or more of ART initiation.
2. To determine factors leading to elevation of viral load among HIV infected individuals after being on ART for six months or more in Pwani region**.**
3. To assess the reasons for non-adherence among study participants.

CHAPTER TWO

2.0 Literature review

Combination therapy of three classes of HIV medications have been widely used in treatment of HIV infection including NRTIs, NNRTIs and PIs (16). Despite of the availability of effective treatment options, suboptimal adherence to the treatment may result into insufficient viral suppression and promote the emergence of drug-resistant viral strains, resulting in regimen failure, progression to AIDS and death (35). In sub-Saharan Africa, more than 25 % of patients using ART, may not achieve viral suppression by 12 months after ART initiation (36). Factors associated with elevation of viral load can be categorized into seven domains: patient factors (predisposing, enabling, perceived need), health care environment factors (system, clinic, provider), and external environment. Predisposing factors are characteristics of the patient that are unlikely to change (e.g. mental illness), enabling factors are resources that encourage health behaviors (e.g. social support), and perceived need relates to beliefs and values affecting subjective acknowledgment of need (e.g. symptoms) (37)**.**

A qualitative analysis data obtained from 51 people living with HIV (PLWH) identified 18 barriers affecting retention and ART adherence. The barriers were as follows eleven factors were common to both behaviors (mental illness, substance abuse, stigma, insurance, social support, housing, reminder strategies, competing life activities, symptoms, co-location of services and provider factors) (38)**.** Three were specific to retention (appointment scheduling, clinic experiences, transportation), and four were specific to adherence (pharmacy services, medication characteristics, health beliefs, health literacy). Other studies focusing on underserved populations (women, low income) have identified similar factors affecting retention such as patient/provider relationships, social support, transportation, and stigma (39–41). These findings indicate that multiple factors, ranging from the patient to the external environment can impact both retention and adherence.

PLWH have different predisposing factors, which can be significant barriers to health behaviors because patients may struggle with their own health during these active periods. Social support from family, friends, and neighbors who are aware of patients' HIV status can help patients maintain clinic visits and medication adherence, as these supports often

provide moral encouragement and health care assistance through transportation and reminders (40). Based on survey data from a representative sample of PLWH in New York City between 1994 and 1997, social support was associated with improved adherence to ART among those who disclosed their HIV status to household members or friends and acquaintance networks (40)**.**

Patients who adopt reminder strategies such as using alarms, calendars, and pillboxes are less likely to forget appointments and medication doses (42,43). Having a medication regimen with low pill burden, small pill sizes, and minimal adverse effects facilitates adherence because these characteristics are more pleasant to patients, especially those who have difficulty swallowing pills (40,44). In a meta-analysis of randomized controlled trials comparing once-daily versus twice-daily ART regimens, lower pill burdens and once-daily regimens were independently associated with improved adherence (40). Structural factors such as transportation, housing, and insurance, can influence a patient's ability to attend appointments and adhere to treatment.

Lack of affordable transportation is often cited as a major reason for missing clinic appointments (39–41). With unstable housing, comes lack of privacy and increased vulnerability to theft and loss of medications. Patients may fear status disclosure by taking medications in the presence of others, and are therefore more likely to skip doses if they cannot secure a private space (45). In a systematic review of the impact of housing status on health-related outcomes among PLWH, a positive association was found between increased housing stability and outcomes such as medication (40).

Adherence, use of health and social services, health status, and HIV risk behaviors' in all included studies (32,40). Moreover, the cost of medical care and medications can be major barriers for patients, compromising clinic attendance and prescription fills (39,40,45,46) although in our setting most of services for PLWH are provided free of charge.

The health care environment such as pharmacy services, clinic experiences, and patient/provider relationships can significantly impact retention and adherence. Pharmacy characteristics such as unprofessional staff and limited hours can discourage patients from refilling medications promptly (39,40,45,46). However, special services such as home delivery and reminder calls can improve convenience for patients and facilitate adherence (40,47).

Furthermore, provision of medication management by an HIV clinical pharmacist has been shown to improve adherence and clinical outcomes (48). In a retrospective cohort study involving 75 patients where pharmacists provided recommendations on ARV regimen changes, medication adherence (measured by pharmacy refill records) increased from 81% to 89% with pharmacist intervention. Clinical outcomes, such CD4+ cell count and viral suppression, also improved statistically when pharmacists intervened (48).

Clinics with discourteous staff and complicated appointment scheduling and referral processes may deter patients from returning (45,49,50). While, providers who gain patients' trust, are responsive, display empathy, and provide individualized care can encourage both retention and adherence among patients (26,40). In an analysis of patient perceptions of provider attitudes, those with a gap in care of more than one year were more likely to perceive that the provider didn't listen carefully to them or disliked caring for HIV-infected people (30).

CHAPTER THREE

3. 0. METHODOLOGY

3.1 Study Design

We conducted analytical cross sectional study in cohort of Patients taking ARV attending in three council hospitals in Pwani region. We reviewed the viral load electronic database to identify individuals who had tested for viral load six months after initiation of viral load. Patients whose results were reviewed from the database were then recruited to participate in the study whereby they were interviewed to determine factors associated with elevated viral load. And patient included in the study were tested again after six months of using antiretroviral therapy.

3.2 Study Area

The study was conducted in three council hospitals in Pwani region named Kisarawe, Mkuranga and Bagamoyo selected randomly from eight council hospital started offer HIV viral load test. Pwani region is located along the shore of Indian Ocean. The prevalence of HIV in Pwani region was estimated to be over 5.9% (51). Pwani region has a total of approximately 21,545 HIV infected adult patients and 12,623 children who are on ART (51).

3.3 Study period

This study was conducted for a period of 11 months from June 2016 to May 2017**.**

3.4 Study Population

This study included HIV infected patients attending CTC in the three hospitals (Kisarawe, Mkuranga and Bagamoyo), eligible for viral load testing. These hospitals were selected because they started to provide services for viral load testing in June 2016.

3.5 Inclusion criteria

1. HIV infected individuals' who had been on ART for at least six months or more and with viral load above 1000 copies/mL.

2. Patients who consented to participate in this study.

3.6 Exclusion criteria

The sampling excluded the following individuals

1. Resident of Pwani region enrolled for CTC services at any of the selected health facilities but was very sick and had impaired communication.
2. HIV infected patient on ART for six months or more with viral load below 1000 copies/mL
3. Patients who refuse to provide consent.

3.7 Sample Size calculation

The outcome of interest for this study is the elevated viral load after initiation of ART. The study population included individuals already on ART for at least 6 months or more. It has been reported that patients might be on ART for up to 12 months and still have elevated viral load. In the African regions this is estimated to be over 25% of patients on ART (36). Patients included in this study were monitored for viral load again after a period of 6 months, which makes the period on ART about 12 months. In many settings in Tanzania criterion for initiation of ART based on test and treat if you found HIV positive they initiate ARV. The sample size was therefore calculated using the following formula (Daniel, 1999):

$$n = deff + \frac{Z^z P\,(1-P)}{d^2}$$

where, Z = Z statistic for 95% confidence level, with a value of 1.96, P= Expected prevalence of HIV infected individuals who will still have viral load above 1000 copies/mL even after using ART for 12 months, which is taken to be 25% (36), d is the relative precision. The sample size was adjusted for the finite population of 15000 individuals. The average size of clients with our inclusion criterion at most district/council hospitals was used for this adjustment. To account for cluster variation between the hospitals, the sample size was weighted by a design effect, deff of 1.5. Using this information, the minimum sample size was estimated at 434 individuals. A non-response rate was approximated at 10% hence the sample size was adjusted to 482.

3.8 Pretesting of the tool

The structured questionnaires were pre-tested at Mlandizi health center in Kibaha District council (a health facility which is not involved in the study) and research assistants were trained on data collection tool, interview techniques and reviewing of records of HIV infected individuals. Questionnaires were cross-checked for completeness and consistence of the responses before releasing an interviewee. No change made to questionnaires.

3.9 Recruitment and training of research assistants

Three research assistants (Medical doctor/nurses/clinical officer and counselors) who were conversant with CTC services were recruited and trained for one day on data collection tools, interviewing techniques and verification of the viral load from the records.

3.10 Data collection procedures

A structured questionnaire was used to collect socio-demographic information and information on factors associated with elevated viral load among HIV infected individuals. Viral load data (i.e. viral load result/test obtained after period of six month or more after ART initiation) including viral load, types of drug used was obtained retrospectively from the HIV clinic database CTC 2 card. After obtaining informed consent from the study participants and fill a structured questionnaire the blood was drawn for viral load test.

3.11 Laboratory procedures

3.11.1 Specimen collection and transportation

Viral load testing was performed using plasma samples collected from participants who were on ART for at least six months or more since ART initiation. Five milliliters of blood were collected in purple tubes with EDTA as an anticoagulant. Samples were centrifuged at 3000 rpm to get plasma and aliquot into two parts 1.5 mls to 2mls of plasma in case one aliquot fails to provide results and kept at -20^{o}C before being transported in cool box to maintain frozen condition to NHL-QATC for viral load testing.

3.11.2 Viral load testing

Viral load testing was performed using the COBAS AmpliPrep/COBAS TagMan HIV-1 Test v 2.0 according to manufacturer instructions. This is nucleic acid amplification test for the quantitative of HIV-1 RNA in human plasma. COBAS AmpliPrep/COBAS TagMan HIV-1 Test v 2.0 based on three major processes namely HIV-1 RNA isolation, reverse

transcription of the target RNA to generate complementary DNA (cDNA) and simultaneous PCR amplification of target cDNA and detection of cleaved dual labeled oligonucleotides detection probe specific target.

3.12. Data management and analysis

3.12.0 Variables

3.12.1 Dependent variable

Elevated viral load was the dependent variable.

3.12.2 Independent variables

Socio demographic data including age, sex, marital status, level of education, occupation status, area of residence (distance from health facility), and disclosure status, medication, psychosocial support groups, social factor, heath care system, nutrition and food security, transportation, was assessed as independent variables

3.12.3 Data quality

Questionnaires were cross-checked for completeness and consistence of the responses before releasing an interviewee.

3.12.4 Data analysis

Data was entered through Ms. Access and cleaned using Epi Info 3.5.1 software and analyzed using the same software. Categorical variables were summarized using frequency distributions while continuous variables were summarised using measures of central tendency and variability (median and range). The association between the dependent variable (elevated viral load) and independent variables was assessed using chi-square or fisher's exact test which ever applicable. P-value < 0.05 will consider as statistically significant. Factors with p-value ≤ 0.2 at bivariate level were entered into Multiple Logistic Regression Model to identify the independent factors associated with elevated viral load among HIV infected individuals while controlling for potential confounders.

3.13 Ethical considerations.

Ethical clearance for conducting this study was obtained from the MUHAS Senate of research and Publication Committee and Institutional Review Board. Permission for conducting this research in Pwani region was obtained from Regional administrative office as well as respective district medical officers and participating health facilities in-charges.

Participant's names were not included in the data collection tool in order to maintain confidentiality but CTC number were used to identify the participants and linking information from their records. Written informed consent was obtained from all participants before enrollment to the study. Participants were assured that their participation in this study was voluntary and they were free to withdraw any time without any negative impact in their treatment at the clinic. Participants who were found to have raised viral load were linked to CTC for enhanced drug adherence counseling for three months and then monitored for another six months**.**

CHAPTER FOUR

4.0 RESULTS

4.1 Socio demographic characteristics of the study participants (N=482)

A total of 482 HIV infected individuals were recruited into the study. The median age of the study participants was 40 years with range from 15-75 years. Most of the study participants 335 (69.5%) were female, majority of them 149 (30.9%) were those of age group between 35- 44 years. About two third 319 (66.2%) of the participants had primary education level, 188 (39%) were married, and 222 (46.1%) were self-employed. More than half 286 (59.3%) were living in the household that had less than five people. A high proportion of study participants 447 (92.7%) reported to have disclosed their HIV status to one of their family members. Other Socio demographic characteristics are summarized in Table 1.

Table 1: Socio-demographic characteristics of the study participants (n=482)

Variable		Number	Percentage
Age group	<18	41	8.5
	18-24	19	3.9
	25-34	87	18
	35-44	149	30.9
	45-54	115	23.9
	55+yrs	71	14.7
Sex	Male	147	30.5
	Female	335	69.5
Education	Informal	112	23.2
	Primary	319	66.2
	Secondary	47	9.8
	Tertiary	4	0.8
Marital status	Married	188	39
	Cohabiting	6	1.2
	Divorced/Widowed	115	23.9
	Separated	65	13.5
	Single/Never married	108	22.4
Occupation	Student	34	7.1
	Employed	37	7.7
	Self-employed	222	46.1
	Peasant	101	21.0
	Housewife/unemployed	88	18.3
Number of Children	<5	398	82.6
	≥5	84	17.4
Household size/Family member	<5	286	59.3
	≥5	196	40.7
HIV Status Disclosed	Yes	447	92.7
	No	35	7.3
To whom status disclosed	Father	32	6.6
	Mother	163	33.8
	Spouse	97	20.1
	Other(friends, relatives)	190	39.4

Nearly two third of the study participants 306 (63.5%) were living in urban areas. Most of them had permanent residence 388 (80.5%). The majority 344 (71.3%) lived a distance of up to 10 kilometers to the health facility, whereas 263 (54.4%) use more than one hour to reach health facility and majority use public transport 364 (75.5%) (Table 2).

Table 2 Participant's residence and means of transportation to the health facility (n=482)

Characteristics		Number	Percentage
Area of residence	Rural	176	36.5
	Urban	306	63.5
Permanence of Residence	Yes	388	80.5
	No	94	19.5
Ownership of residence	Owns house	317	65.8
	Tenants	75	15.6
	Employee Staff House Scheme	21	4.4
	Don't have residence	69	14.3
Distance from home to Health Facility	<2km	45	9.3
	2 - <5	81	16.8
	5 – 10km	218	45.2
	>10	138	28.6
Time taken from home to health facility	<1 hour	219	45.6
	>1hour	263	54.4
Means of transport	Walking	59	12.2
	Public transport	364	75.5
	Motorcycle/bicycle	53	11.0
	Private transport	6	1.2

4.2 Plasma viral load level after six month of ART use and viral load tested 12 months or more of ART use.

Medical records of 482 participants were reviewed and median plasma viral load tested after six months or more of ART use was found to be 12368 copies/mL (IQR=3999-47236). The median plasma viral load after 12 months or more of use ART (viral load tested six months later after the first viral load measurement) decreased significantly to 437 copies/mL (IQR=20-9303), (p=0.001). A total of 294 (61.0%) study participants were found to have low plasma viral load below 1000copies/mL after 12 months or more of being on ART. Plasma viral load level at six months and at 12 months or more on ART use are summarized in Table 3.

Table 3 Plasma viral load tested after six months and after12 months or more following ART usage (N=482).

	Plasma viral load level after six months or more of ART.		Plasma viral load after12 months or more of ART use.	
Viral load level (Copies/mL)	Number. Participants	Percentage	Number. Participants	Percentage
<1000	-	-	294	61.0
1001-10,000	225	46.7	70	14.5
10001-20000	52	10.8	24	5.0
20001-30000	37	7.7	27	5.6
30001-40000	34	6.8	18	3.70
40001-50000	19	3.9	10	2.10
>50000	116	24.1	39	8.1
Median (IQR)	12368 (3999-47236)		437 (20-9303)	

Elevated viral was defined as a plasma viral load ≥1000 copies/mL

4.3 Medical and Nutritional history of the study participants

Regarding food availability, more than half of the participants 284 (58.9%) reported to be able to get three or more meals per day for the past one year. Less than quarter of the subject 89(18.5%) failed to take drugs on empty stomach, while 96 (19.9%) were unable to take medication in the presence of people. as related to alcohol consumption, 76 (15.8%) of participants reported to drink alcohol one to five times in a week. The majority of

participants attended enhanced adherence counseling (EAC) after receiving viral load results of more than1000 copies/ mL (Table 4).

Table 4 Medical and Nutritional history of the study participants (n=482)

Characteristics		Number	Percentage
Meals taken per day	Single meal	17	3.5
	Two meals per day	181	37.6
	Three/more meals per day	284	58.9
Drinking alcohol	Never take alcohol	406	84.2
	One or less a week	39	8.1
	Two to five times a week	37	7.7
Fail to take drug on empty stomach	Yes	89	18.5
	No	393	81.5
Dose frequencies	Single dose per day	281	58.3
	Twice per day	201	41.7
Experience drug side effects	Yes	117	24.3
	No	365	75.7
Which side effects experienced	Anemia & Nephrotoxicity	9	7.7
	Hypersensitivity	78	66.7
	Other	30	25.6
Failure to take medication in presence of people	Yes	96	19.9
	No	386	80.1
Member of psychosocial support group	Current	36	7.5
	In past	12	2.5
	Never been	434	90.0
Attended EAC* when results ≥1000cp/ml	Yes	425	88.2
	No	57	11.8
Types of ART used	First line	435	90.30
	Second line	47	9.70

*EAC –Enhanced adherence counseling

4.4 Reasons for non-adherence among the study participants

Being too much occupied with work to take their drugs or forgetting 159 (33%) were the most frequent cause mentioned for non-adherence among the HIV infected patients on ART. Other reasons for non-adherence are as shown in Figure 1.

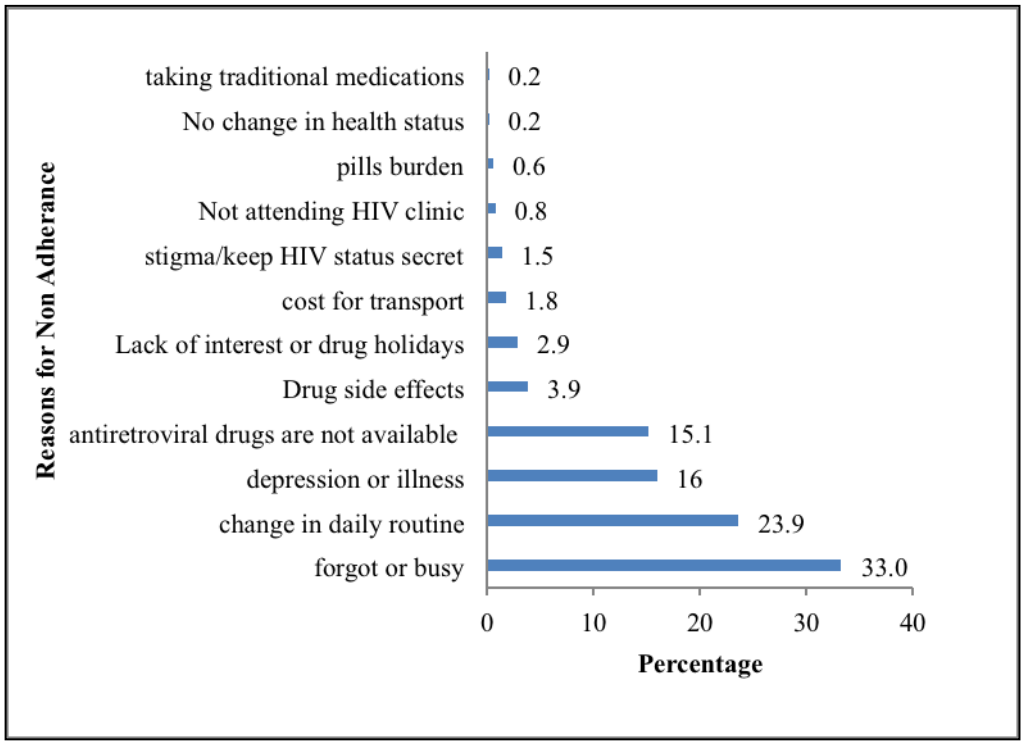


Figure 1. Reasons for non-adherence among HIV Infected Individuals (n=482)

4.5. Factors influencing elevated viral load among the study participants receiving ART in Pwani region.

Bivariate level analysis

HIV infected individuals aged below 35 years old had 1.5 times odds of having high viral load compared to those aged above 35 years old ($p<0.034$). The HIV infected individuals who were not living with partners had 1.60 times odds of having elevated viral load than those living with partner ($p<0.02$).

The HIV infected individuals who did not disclose their HIV status had 3.78 times odds of having elevated viral load results than those who disclosed their HIV status ($p<0.002$). Individuals who reported not to have a permanent residence had 2.17 times odds of having

elevated viral load than those who had no permanent residence ($p<0.001$). The HIV infected individuals who fail to take medication in presence of people or family member had 2.29 times odds of having elevated viral load than those who had the ability to take medication even in the presence of people ($p<0.0002$). Those who did not attend enhanced adherence canceling (EAC) had 3.08 times odds of having elevated viral load than those who attended EAC ($p<0.0001$). Participants who reported to take alcohol had 3.49 times odds of having elevated viral load than those who were not taking alcohol ($p<0.0001$). Individuals who reported not to be member of psychosocial support groups had 2.64 times odds of having high viral load than those who attended the psychosocial support groups ($p<0.006$). Those who reported to have few number of meals per day had 1.64 times odds of have elevated viral load than those with adequate food intake ($p<0.009$). Individual who experienced stigma had 0.63 times odds of having elevated viral load compared to those who did not experience stigma ($p<0.0001$). Failure to take medication in empty stomach had four times odd of having elevated viral load compared to those who took medication even in an empty stomach ($p<0.0001$). Participants with primary education level or below were more likely to have elevated viral load than those with secondary education level or above but the difference was not statistically significance ($p<0.57$) see (Table 5).

Table 5 Factors influencing the elevated viral load among HIV infected individuals receiving ART 12 months or more after initiation of ART in Pwani Region.

Characteristics		Viral load		OR (CI 95%)	P-value
		>1000copies/mL	< 1000copies/mL		
Age below 35	Yes	80 (45.2)	97 (54.8)	1.5(1.03- 2.19)	0.034*
	No	108 (35.4)	197 (64.6)		
Sex	Male	65 (44.2)	82 (55.8)	0.73(0.65-2.19)	0.33
	Female	123 (36.7)	212 (63.3)		
Low education	Yes	170 (39.4)	261 (60.6)	1.19(0.76-1.65)	0.57
	No	18 (35.3)	33 (64.7)		
Not living with partner	Yes	125 (43.4)	163 (56.6)	1.59(1.09- 2.33)	0.02*
	No	63 (32.5)	131 (67.5)		
Unemployed	Yes	97 (43.5)	126 (56.5)	1.42(0.98-2.05)	0.061
	No	91 (35.1)	168 (64.9)		
HIV status disclosed	Yes	24 (68.6)	11 (31.4)	3.78(1.78-7.88)	0.0002*
	No	164 (36.7)	283(63.3)		
No permanent residence	Yes	51 (54.3)	43 (45.7)	2.17(1.38- 3.43)	0.001*
	No	137(35.3)	251 (64.7)		
Did not attended EAC	Yes	36 (63.2)	21 (36.8)	3.08(1.74 – 5.46)	0.0001*
	No	152 (35.8)	273(64.2)		
Taking Alcohol	Yes	49 (64.5)	27 (35.5)	3.49(2.09 – 5.82)	0.001*
	No	139 (34.2)	267 (65.8)		
Few number of meals per day	Yes	91 (46.0)	107 (54.0)	1.64(1.13 – 2.38)	0.01*
	No	97 (34.2)	187 (65.8)		
Experience stigma	Yes	84(51.9)	78(48.1)	0.63(0.51-0.78)	0.0001
	No	104 (32.5)	216 (67.5)		
Not member of psychosocial support	Yes	178 (41.0)	256 (59.0)	2.64(1.28 – 5.44)	0.01*
	No	10 (20.8)	38 (79.2)		
Fail to take medication in presence of people	Yes	53 (55.2)	43 (44.8)	2.29(1.46 – 3.61)	0.0003*
	No	135 (35.0)	251 (65.0)		
Fail to take medication in empty stomach					
	Yes	59 (66.3)	30(33.7)	4.03(2.47 – 6.55)	0.001*
	No	129 (32.8)	264(67.2)		

*Statistically significant (p=<0.05)

Multivariate level

Factors that influenced the elevation of viral load with p value ≤ 0.2 at bivariate level were included in multivariate analysis (Table 5). After adjusting for confounding variables, factors that remained to be significantly associated with elevated viral load were as follows; HIV infected individuals who had not disclosed their HIV status were three times more likely to have elevated viral load compared to those who disclosed their HIV status (OR=2.73 95% CI (1.19-6.24). HIV infected individuals who did not attend enhanced adherence counseling were three times more likely to have elevated viral load compared to those who attended (OR= 3.27 95% CI (1.75- 6.09). Those who reported to be taking alcohol were almost three times more likely to have elevated viral load compared to those who reported not to be taking alcohol (OR=2.57 95% CI (1.44 - 4.59). Moreover, individuals who were not members of psychosocial groups were almost three times more likely to have elevated viral load compared to those who were members of psychosocial groups (OR=2.67 95% CI (1.22-5.82). Participants who reported to take two meals or less per day were two times more likely to have elevated viral load compared to those who reported to take three or more meals per day (OR= 1.62 95% CI (1.07-2.44). HIV infected individuals who could not take medication on an empty stomach were almost four times more likely to have elevated viral load compared to those who were able to take medication even on empty stomach (OR= 3.56 95% CI (2.12- 5.98). Other factors are shown on table below (Table 6).

Table 6 Multivariate logistic analysis of factors influencing elevated viral load

Characteristics		OR	CI (95%)	P-value
Age below 35 (No=Ref)	Yes	1.44	(0.99-2.01)	0.056
Sex (Female=Ref)	Male Female	1.38	(0.93-2.04)	0.112
Not living with partner (No= Ref)	Yes	1.31	(0.87-1.99).	0.20
Unemployed (No=Ref)	Yes	1.33	(0.88-2.0)	0.17
HIV status disclosed (No=Ref)	Yes	2.73	(1.19-6.23)	0.02*
No permanent residence (No=Ref)	Yes	2.09	(1.33-3.31)	0.001*
Fail to take medication presence of people	Yes	1.38	(0.76-2.27)	0.37
Not attending EAC session (No=Ref)	Yes	3.27	(1.75-6.09)	0.0002*
Drinking alcohol (No=Ref)	Yes	2.57	(1.44-4.59)	0.002*
Not member of Psychosocial group (No=Ref)	Yes	2.67	(1.29-5.49)	0.01*
Few number meals per day (No=Ref)	Yes	1.62	(1.07-2.44)	0.02*
Fail to take medication in empty stomach (No= Ref)	Yes	3.56	(2.11-5.98)	0.001*

CHAPTER FIVE

5.1 DISCUSION

This study aimed to determine the factors that led to elevated viral load among HIV infected individuals receiving ART in Pwani Region. We found a high proportion (39%) of individuals having elevated viral load despite being on ART treatment for 12 months or more. The median plasma viral load was high (12368 copies/mL) after the first six months or more of ART, which decreased significantly to 437 copies/mL six months later i.e.12 months from ART initiation. In this study, drinking alcohol, not attending EAC session, failure to take medication in empty stomach, consuming little number of meals per day, not being a member of psychosocial group and failure to disclose their HIV status were the common factors associated with elevated viral load among HIV infected patients on ART. This finding is similar to study done by Gebrezgabheer et al who reported that a detectable viral load after ART use is an indication of poor adherence, thus timely identification of viremia is very crucial as it provides an opportunity to reinforce adherence before the development of resistance which is needed to maintain the efficacy of the patient's current antiretroviral therapy(53)An effective ART results into decrease of plasma viral load, enhance immune recovery and therefore increase in number of $CD4^{+}$cell counts. According to guideline for monitoring of ART response by Ministry of Health prepared by NACP, it's expected that viral load to decrease to less than 1000 copies/mL following ART for six months or more (1).

Despite the availability of effective treatment option, suboptimal adherence to the treatment may result into insufficient viral suppression and promote the emergence of drug resistance viral strains, resulting in regime failure, progression to AIDS and death (54). In the current study the plasma viral load results obtained after the period of six months or more following ART initiation was high, 12368copies/mL. However, following the enhanced adherence counseling to the patients and close follow up by health worker there was a significant viral suppression to median viral load of 437copies/mL indicating that there is a need to enroll patients in the adherence and counseling at the time of ART initiation. The median viral load obtained in this study was higher than the median viral load (6985 copies/mL) reported in the study done in Mbeya Tanzania where the viral load

was tested before the ART initiation. The median viral load observed in this study is above the limit recommended by national AIDS control program target in Tanzania (i.e., 1000copies/mL) which is not acceptable for individuals taking ART for the duration of six month or more (1, 23). Several factors associated with elevated viral load among HIV infected individuals on ART have been reported in the other studies (55). Failure to disclose HIV status has negative impact, making it difficult for patients to take their medication timely and regularly. In the present study, patients who fail to disclose their HIV status had three times high risk of having elevated viral load compared to those who disclose their HIV status. These finding are similar with those found elsewhere where fear to disclosure the HIV status was the considerable barrier (9,26,40,41,44). We also found that individuals who drink alcohol had three times risk of having elevated viral load compared to those not taking alcohol. Similarly to study conducted by Holtzman et al in Lesotho reveal that individuals who were taking alcohol had high risk of having elevated viral load compared to those who don't take alcohol (9,40). The reason is that these patients often became apathetic about their health care, which leads to miss appointments and poor medication adherence. Misconceptions about mixing HIV medications and illicit drugs and or alcohol also compromised ART adherence.

Patient who did not attend EAC session were more at risk of having elevated viral load compared to those who attended the EAC session. Similarly individuals who did not join psychosocial group had high risks of elevated viral load compared to those who were members of psychosocial group (23,26,39). These finding concur to those found in Ethiopia and Lesotho which revealed that being a member in psychosocial support group influenced the provision of services that respond to patient medically, psychological and social needs (40,44,58). Therefore special attention is needed to people with limited social support, resources, stigma concerns and concerns about treatment regime as efficacy is warranted in HIV infected people (40).

In relation to non-adherence to treatment, the common reasons mentioned by the respondents was forgetting to take medication or being so busy with work and change of their daily routine. These finding are consistence with other studies done elsewhere where, forgetting or being busy and change in daily activities were among the reasons contribute to elevation of viral load in patients taking ART medication (59). In addition, depression or

other illness among the individuals who has lost hope of being cured was also mentioned as a reason to elevation of viral load levels. These finding concurred with reports from a study conducted in Ethiopia where feeling depressed or other illness contributed to the worsening of HIV related clinical outcomes (60). Furthermore, some of respondents reported that ART was not regularly available at the clinic. Similar finding has been reported elsewhere (43). This study also found that drugs side effects, lack of interest and or drug holidays also contributed to non-adherence to ART. Cost of transportation or lack of bus fare to the health facility was also reported as challenge to most of HIV infected individuals, similar to the finding reported elsewhere (59). Moreover some of respondents reported that stigma and keeping HIV status secret were reasons for non-adherence which can result into elevation of viral load among HIV infected individuals, a finding similar to what was reported in other studies (41,61).

5.2 Study limitation

There was a lack of baseline viral load data of HIV infected individuals before ART initiation, which makes it difficult to compare with plasma viral load level tested six months of ART. According to the guideline by Ministry of Health plasma viral load are measured six months after ART initiation and not before. Monitoring of ART response using plasma viral load level measurement was introduced by MOH, in June 2016. Before that time CD4+ counts was used as criteria for ART initiation as well as for treatment monitoring.

5.3 Conclusion

While ART has made it possible to significantly decrease of HIV related morbidity and mortality, this study found a high proportion (39%) of individual with elevated viral load despite being on ART treatment for 12 months or more. The factors which influence the raise of viral load to patients using ART in Pwani region included taking alcohol, taking few meals per day not attending EAC session, failure to take medication in empty stomach, consuming few number of meals per day, not being a member of psychosocial group and failure to disclose their HIV status. This study also found that feeling depressed or having illness, forgetting or being too much occupied with work, or ART stock out, change in daily routine was among the reasons for non-adherence.

5.4 Recommendation

Emphasis should be made by health-care providers on enhancing adherence and counseling to all HIV infected patients at the time of ART initiation. Patient should also be encouraged by health care providers to join psychosocial group where they will receive psychosocial support to help them cope with fear of HIV disclosure as well as stigma. I recommend that another study should be conducted to assess the possibility of antiretroviral drug resistance biological failure particularly for patients with elevated viral load after 12 months of ART despite being on enhanced adherence and counseling group. Health worker should train on what are indicator or criteria for health worker to decide to shift the patient to second line and is it known to all prescriber in CTC.

6.0 REFERENCES

1. NACP. Tanzania National guidelines for the management of HIV and AIDS. Natl AIDS Control Program. 2015;5th Ed.
2. Palella, Frank J, Kathleen M. Delaney etal. Declining morbidity and mortality among patients with advanced Human Immunodeficience Virus Infection. N Engl J Med. 1998;338(13):853–60.
3. Kirkland LR, Fischl MA, Tashima KT, etal. Response to lamivudine-zidovudine plus abacavir twice daily in antiretroviral-naive , incarcerated patients with HIV Infection Taking Directly Observed Treatment. Clin Infect Dis. 2002;(34):511–8.
4. Zhou S, Martin K, Corbett A, Napravnik S, Eron J, Zhu Y, et al. Total daily pill burden in HIV-infected patients in the southern United States. AIDS Patient Care STDS. 2014;28(6):311–7.
5. Lima, Viviane D,Harrigan R. Bangsberg DR. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. J Acquir Immune Defic Syndr. 2013;50(5):529–36.
6. Pinto M, Silveira T, Draschler MDL. Predictors of undetectable plasma viral load in HIV-Positive Adults Receiving Antiretroviral Therapy in Southern Brazil. Brazilian J Infect Dis Context Publ. 2002;6(4):164–71.
7. Hogg RS, Yip B, Chan KJ etal. Rates of disease progression by baseline CD4 Cell Count and Viral Load After Initiating Triple-Drug Therapy. JAMA. 2016;286(20):2568–77.
8. Hubert JB, Burgard M, Dussaix E, Tamalet C, Deveau C, Le Chenadec J, et al. Natural history of serum HIV-1 RNA levels in 330 patients with a known date of infection. The SEROCO Study Group. AIDS. 2000;14(2):123–31.
9. Tiruneh YM, Galárraga O, Genberg B etal. Retention in care among HIV-Infected Adults in Ethiopia , 2005 – 2011 : A Mixed-Methods Study. PLoS One. 2016;11(6):2005–11.
10. Yerly S, Kaiser L, Perneger T V, Cone RW, Opravil M, Chave JP, et al. Time of initiation of antiretroviral therapy: impact on HIV-1 viraemia. Aids. 2000;14(3):243–9.

11. Gifford, Allen L, Jill E. Bormann, Matha J. Shively etal. Predictors of self-reported adherance and plasma HIV concentration in Patient on Multidrug Antiretroviral Regimes. Jaids. 2000;(23):386–95.
12. Paterson DL, Swindells S, Mohr J, etal. Adherence to protease inhibitor therapy and outcomes in patients with HIV Infection. Ann Intern Med. 2000;(133):21–30.
13. Bangsberg DR, Hecht FM, Charlebois ED etal. Adherence to protease inhibitors , HIV-1 viral load , and development of drug resistance in an indigent population. Aids. 2000;(14):357–66.
14. Rossouw TM, Feucht UD, Melikian G, Van Dyk G, Thomas W, Du Plessis NM, et al. Factors associated with the development of drug resistance mutations in HIV-1 infected children failing protease inhibitor-based antiretroviral therapy in South Africa. PLoS One. 2015;10(7):1–16.
15. Valdez H, Lederman MM, Woolley E. Human Immunodeficiency Virus 1 Protease Inhibitors in Clinical Practice. Arch Intern Med. 1999;159:1771–6.
16. Bezabhe WM, Chalmers L, Bereznicki L etal. Adherence to Antiretroviral Therapy and Virologic Failure. Med J. 2016;95(15):1–9.
17. Harrigan PR, Hogg RS, Dong WWY, Yip B, Wynhoven B, Woodward J, et al. Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. J Infect Dis. 2005;191(3):339–47.
18. Havlir D V, Koelsch KK, Strain MC, Margot N, Lu B, Ignacio CC, et al. Predictors of residual viremia in HIV-infected patients successfully treated with efavirenz and lamivudine plus either tenofovir or stavudine. J Infect Dis. 2005;191(7):1164–8.
19. Hinkin CH, Barclay TR. Drug Use and Medication Adherence among HIV-1 Infected Individuals. AIDS Behav. 2010;11(2):185–94.
20. Saathoff E, Pritsch M, Geldmacher C, Hoffmann O, Koehler RN, Maboko L, et al. Viral and host factors associated with the HIV-1 viral load setpoint in adults from Mbeya Region, Tanzania. J Acquir Immune Defic Syndr. 2010;54(3):324–30.
21. Raffi F, Yazdanpanah Y, Fagnani F, Laurendeau C, Lafuma A, Gourmelen J. Persistence and adherence to single-tablet regimens in HIV treatment: A cohort study from the French National Healthcare Insurance Database. J Antimicrob Chemother. 2014;70(7):2121–8.

22. Palella FJ, Greenblatt RMCJ. Influence of gender on receipt of guideline-based antiretroviral therapy in the era of HAART. AIDS Care. 2013;24(1):20–9.
23. Nsimba SED, Irunde H, Comoro C. Barriers to ARV adherence among HIV/AIDS positive persons taking anti-retroviral therapy in two Tanzanian regions 8-12 months after program initiation. J AIDS Clin Res. 2010;1(3):1–9.
24. Nash D, Katyal M, Shah S. Trends in predictors of death due to HIV-related causes among persons living with AIDS in New York City: 1993-2001. J Urban Heal. 2005;82(4):584–600.
25. Milloy MJ, Marshall BDL, Montaner J, Wood E. Housing status and the health of people living with HIV/AIDS. Curr HIV/AIDS Rep. 2012;9(4):364–74.
26. Mccoy K, Higgins M, Holstad MM etal. Age, stigma, adherence and clinical indicators in HIV-infected woman. HIV/AIDS Res Treat. 2015;SE3(1–8):1–14.
27. McCoy K, Waldrop-Valverde D, Balderson BH, Mahoney C, Catz S. Correlates of antiretroviral therapy adherence among HIV-Infected Older Adults. J Int Assoc Provid AIDS Care. 2016;15(3):248–55.
28. Masquelier B, Peytavin G, Leport C, Droz C, Duran S, Verdon R, et al. Mechanisms of early virologic failure in antiretroviral-naive patients starting protease inhibitor-containing regimens: the APROVIR Study. J Infect Dis. 2002;186(10):1503–7.
29. Maldonado-martínez G, Hunter-mellado RF, Fernández-santos D. Persistent HIV viremia : description of a cohort of HIV infected individuals with ART Failure in Puerto Rico. Enviromental Res Public Heal. 2015;1–8.
30. Magnus M, Herwehe J, Murtaza-Rossini M, Reine P, Cuffie D, Gruber D, et al. Linking and retaining HIV patients in care: the importance of provider attitudes and behaviors. AIDS Patient Care STDS. 2013;27(5):297–303.
31. Liu E, Spiegelman D, Semu H, Hawkins C, Chalamilla G, Aveika A, et al. Nutritional status and mortality among HIV-infected patients receiving antiretroviral therapy in Tanzania. J Infect Dis. 2011;204(2):282–90.
32. Lima V, Anema A, Bangsberg D, Julio S. NIH Public Access. J Acquir Immune Defic Syndr. 2013;52(August 2008):342–9.
33. Li L, Ji G, Liang LJ, Ding Y, Tian J, Xiao Y. A multilevel intervention for HIV-affected families in China: Together for Empowerment Activities (TEA). Soc Sci Med. 2011;73(8):1214–21.

34. Leaver CA, Bargh G, Dunn JR, Hwang SW. The effects of housing status on health-related outcomes in people living with HIV: A systematic review of the literature. AIDS Behav. 2007;11(85–100).
35. Delaugerre C, Rohban R, Simon A etal. Resistance Pro ® le and Cross-Resistance of HIV-1 Among Patients Failing a Non-Nucleoside Reverse Transcriptase Inhibitor-Containing Regimen. J Med Virol. 2001;65:445–8.
36. Rutstein SE, Hosseinipour MC, Weinberger M, Wheeler SB, Biddle AK, Wallis CL, et al. Predicting resistance as indicator for need to switch from first-line antiretroviral therapy among patients with elevated viral loads: development of a risk score algorithm. BMC Infect Dis. 2016;16(1):280–93.
37. Andersen RM. Revisting the behavioral model and access to medical care does it matter? J Health Soc Behav. 1995;36:1–10.
38. R. Paredes, T. Puig CT etal. High-dose saquinavir plus ritonavir: long -term efficacy in hiv possitive protease inhibitor -experienced patients and predictors of virological response. JAIDS. 1999;22:132–8.
39. Hines J, Mounzer K, Metlay JP etal. Mapping Patient–Identified Barriers and Facilitators to Retention in HIV Care and Antiretroviral Therapy Adherence to Andersen's Behavioral Model Carol. AIDS Care. 2015;27(7):817–28.
40. Holtzman CW, Brady KA, Yehia BR, etal. Retention in care and medication adherence: current challenges to antiretroviral therapy success. PMC. 2016;75(5):445–54.
41. Audet CM, Mcgowan CC, Wallston KA, etal. Relationship between HIV stigma and self-isolation among people living with HIV in Tennessee. PLoS One. 2013;8(8):1–8.
42. Petersen ML, Wang Y, Laan MJ Van Der, etal. Pillbox Organizers Are Associated with Improved Adherence to HIV Antiretroviral Therapy and Viral Suppression: A Marginal Structural Model Analysis. Clin Infect Dis. 2007;45(7):908–15.
43. Nachega JB, Parienti J, Gross R, etal. Lower Pill Burden and Once-Daily Antiretroviral Treatment Regimens for HIV Infection : A Meta- Analysis of Randomized Controlled Trials. Clin Infect Dis. 2014;58(9):1297–307.
44. Yehia BR, Stewart L, Momplaisir F, etal. Barriers and facilitators to patient retention in HIV care. BMC Infect Dis. 2015;15:1–10.

45. Rozanova J, Brown S, Bhushan A, etal. Effect of social relationships on antiretroviral medication adherence for people living with HIV and substance use disorders and transitioning from prison. Heal Justice. 2015;3(18):1–13.
46. Ford MA, Spicer CM. Monitoring HIV Care in the United States: Indicators and Data Systems. 2012. 127-159 p.
47. DuChane J, Clark B, Hou J, Fitzner K, Pietrandoni G, Duncan I. Impact of HIV-specialized pharmacies on adherence to medications for comorbid conditions. J Am Pharm Assoc. 2014;54(5):493–501.
48. Ma A, Chen DM, Chau FM etal. Improving adherence and clinical outcomes through an HIV pharmacist's interventions. AIDS Care. 2010;22(10):1189–94.
49. Sevelius JM, Patouhas EKJ. etal. Barriers and Facilitators to Engagement and Retention in Care among Transgender Women Living with Human Immunodeficiency Virus. Ann Behav Med. 2015;47(1):5–16.
50. Samina T. SYED ,Ben S. gerber LKS. Traveling Towards Disease: Transportation Barriers to Health Care Access. j Community Heal. 2013;38(5):976–93.
51. NACP. HIV / AIDS / STI Surveillance Report. Vol. 1. 2015. 10 p.
52. James H McMahon, Julian H Elliott, Silvia Bertagnolio RK& MRJ. Viral suppression after 12 months of antiretroviral therapy in low. 2013;(91):377–85.
53. Gebrezgabher BB, Kebede Y, Kindie M, Tetemke D, Abay M. Determinants to antiretroviral treatment non ‐ adherence among adult HIV / AIDS patients in northern Ethiopia. AIDS Res Ther. 2017;14(16):1–7.
54. Yehia BR, French B, Fleishman JA. Retention in Care is More Strongly Associated with Viral Suppression in HIV-Infected Patients with Lower versus Higher CD4 Counts. J Acquir Immune Defic Syndr. 2015;65(3):333–9.
55. Bonner K, Mezochow A, Roberts T, Ford N, Cohn J. Viral load monitoring as a tool to reinforce adherence: a systematic review. J Acquir Immune Defic Syndr. 2013;64(1):74–8.
56. Saberi P, Dong BJ, Johnson MO, Greenblatt RM, Cocohoba JM. The impact of HIV clinical pharmacists on HIV treatment outcomes: A systematic review. Patient Prefer Adherence. 2012;6:297–322.

57. Guglielmo BJ, Pharm D. Improved antiretroviral refill adherence in HIV-focused community pharmacies. J Am Pharm Assoc. 2015;52(2003):1–13.
58. Saint-Jean G, Metsch L, Gomez-Marin O, Pierre C, Jeanty Y, Rodriguez A, et al. Use of HIV primary care by HIV-positive Haitian immigrants in Miami, Florida. AIDS Care. 2011;23(4):486–93.
59. Chesney M. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis. 2000;30(Suppl 2):S171–6.
60. Vogenthaler NS, Hadley C, Lewis SJ, Rodriguez AE, Metsch LR, Rio C. Food insufficiency among HIV - infected crack - cocaine users in Atlanta and Miami. AIDS Behav. 2015;13(9):1478–84.
61. Magnus M, Herwehe J, Murtaza-Rossini M, Reine P, Cuffie D, Gruber D, et al. Linking and retaining HIV patients in care: the importance of provider attitudes and behaviors. AIDS Patient Care STDS. 2013;27(5):297–303.

7.0 APPENDIX

Appendix 1a: INFORMED CONSENT FORM- English Version

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

Title: To determine the predictors of elevated viral load among HIV infected adults receiving ART in Pwani region Tanzania.

ID-NO _____

Consent to participate in this study

Greetings, my name is …..... from Muhimbili University of Health and Allied Sciences, Dar es Salaam. We are carrying out a study to determine the predictors of elevated viral load among HIV infected adults receiving antiretroviral therapy in Pwani region, Tanzania

Purpose of the study

This study aims to collect information on factors associated with elevation of viral load among HIV/AIDS infected adults receiving antiretroviral therapy. You are being asked to participate in this study as stakeholder and a resident from the study site. We will be grateful if you will allow us to use your data from CTC2 database and CTC2card to obtain patient information.

Confidentiality

I assure you that all the information collected from CTC 2 database and CTC2 card will be kept confidential. Only people working in this research study will have the access to the information. We will ensure that any information collected from the patient file does not identify the patients name or other identifying information on the records of the information we will collect.

Risks

No any risk is foreseen in this study.

Benefits

The information you provide to us is extremely important and valuable. It will help policy maker and other health official at every level to improve or otherwise rectify logistics and circumstances in favor of service utilizer's. There are no direct benefits however; individual benefit it will be obtained through intervention programs, which can be conducted in this particular area.

In case of injury

We are not anticipating that any harm will occur as the result of data collection in this study

Who to Contact

If you ever have questions about this study, you should contact the study Coordinator or the Principal Investigator Josiah Isaac Mutigitu Muhimbili University College of Health Sciences, P.O.Box 65001, Dar es Salaam).

If you ever have questions about your rights as a participant, you may call Dr. Joyce Rose Masalu, Acting Chairperson of the Senate Research and Publications Committee, P.O. Box 65001, Dar es Salaam. Tel: 2150302-6, 2152489.

Do you agree?

Participant agrees…… Participant does not agree…….

I …….have read the content in this form, my questions have been answered, I agree to participate in this study

Signature of Participant……..……..…

Signature of Research assistant……..……

Date of signed consent……

Appendix 1b: INFORMED CONSENT (Kiswahili Version)

CHUO KIKUU CHA SAYANSI ZA AFYA MUHIMBILI-

Kichwa cha habari:……..

Namba ya Utambulisho……./……./…….

Ridhaa ya kukusanya takwimu kwa utafiti huu

Habari!

Jina langu naitwa……na toka Chuo Kikuu cha Sayansi za Afya Muhimbili, Dar es salaam. Tunafanya utafiti utakao tuwezesha kutambua sababu zinazopelekea kuongezeka kwa viwango vya virusi katika damu kwa wagonjwa wanaotumia dawa zakupunguza makali ya virusi vya ukimwi (ARV) Kwa watu wazima katika mkoa wa Pwani Tanzania.

Lengo la utafiti

Utafiti huu unalengo la kukusanya taarifa zitakazoelezea Kutambua sababu zinazopelekea kuongezeka kwa viwango vya virusi kwa wagonjwa wanaotumia dawa za kufubaza makali ya virusi vya ukimwi (ARV) ilikufanikishwa kwa huduma ya kupunguza makali VVU kwa watu wazima katika mkoa wa Pwani Tanzania.

Usiri

Nakuhakikishia kwamba taarifa zote zitakazokusanywa kutoka katika kadi ya CTC zitakuwa ni siri, Ni watu wanaofanya kazi katika utafiti huu tu ndio wanaweza kuziona taarifa hizi. Tunakuakikishia ya kwamba taarifa zitakazo jumuishwa kwenye ripoti yetu hazitakuwa zinatoa au zinatambulisha mgonjwa. Hatutaweka jina la mgonjwa au taarifa yoyote ya utambulisho kwenye kumbukumbu ya taarifa tutakazoandika.

Madhara

Hakuna madhara yeyote yanayotegemewa kutokea kutokana na utafiti huu.

Faida

Taarifa utakayotupatia nimuhimu sana na yenye thamani kwa kuwa itasaidia kuongeza uelewa wetu kuhusu ufahamu,wa sababu zinazopelekea kuongeze kakwa viwango vya virusi kwa wagonjwa wanaotumia dawa za kufubaza makali ya virusi vya UKIMWI

katika kliniki ya huduma katika mkoawa Pwani Pia taarifa utakayo tupatia itasaadia kuandaa sera nampango mkakati a kuhakikisha wagonjwa wote wanaoanza kutumia dawa katika kipindi cha ndani ya miazi sita wawe wanabaki kiwango cha chini cha viwango vya virusi, kwa muda wote nakuboresha huduma ya kuthibiti maambukizi ya VVU kwa watu wasionayo.

Endapo utaumia

Hatutegemei madhara yeyote kutokea katika ukusanyaji wa takwimu katika utafiti huu.

Watu wakuwasiliana nao

Kama unamaswali katika utafiti huu usisite kuwasiliana nasi

Josiah Isaac Mutigitu, Mtafiti mkuu, Chuo Kikuu Cha Afya Muhimbili, S.L.P 65001, Dar es salaam(Simu no. 0715600930)

Kama unamaswali kuhusiana na haki zako kama mshiriki katika utafiti huu. Dr. Joyce Rose Masalu, Acting Chairperson of the Senate Research and Publications Committee, P.O. Box 65001, Dar es Salaam. Tel: 2150302-6, 2152489.

Je, Umekubali?

Mshiriki amekubali…… Mshiriki hajakubali……

Mimi……...nimesoma maelezo ya fomu hii, maswali yangu yamejibiwa na nimeridhika.Nakubali kushiriki katika utafiti huu.

Sahihi ya Mshiriki……

Sahihi ya mtafiti msaidizi…….

Tarehe ya kutia sahihi ya kushiriki……..

Appendix 2a: QUESTIONNAIRE (ENGLISH VERSION)

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

Title: To determine the predictors of elevated viral load among HIV infected adults receiving ART in Pwani region Tanzania.

PART A: Socio-demographic.

1. Date of interview……..
2. ID number…….
3. Name of the facility /CTC.....
4. Name of the district ……..
5. Level of the facility
    a) Hospital
    b) Health Centre
6. Ownership of the health facility
    a) Public
    b) FBO
    c) Private
7. Age of the participants.....
8. Sex
    a) Male
    b) Female
9. Level of education.
    a) No formal education
    b) Primary education
    c) Secondary education
    d) Tertiary
10. Occupation of the Participants
    a) Employed
    b) Housewife
    c) Peasant
    d) Businessman/businesswoman

11. Marital status of the participants.
    a) Single
    b) Married
    c) Cohabiting
    d) Divorced/widowed
    e) Separated
12. How many children do you have? .....
13. How many members are in your family? .....
14. Have you ever disclose your status to any member of the family or friends.
    a) Yes
    b) No
15. If yes from Q14 specify who know your HIV status……
    a) Spouse
    b) Mother
    c) Father
    d) Other
16. Area of residence
    a) Urban
    b) Rural
17. Distance from home to health facility
    a) <2km
    b) 2-5km
    c) 5-10km
    d) Above 10km
18. How long do you use to reach clinic from where you stay……..…
19. Which means of transport do you use to go clinic?
    a) A walking distance
    b) Use of motor cycle/Bicycle
    c) Use public transport.
    d) Use private transport

PART B: ADHERENCE AND FACTORS ASSOCIATED WITH INCREASE OF VIRAL LOAD AMONG HIV INFECTED ADULTS RECEIVING ART IN PWANI REGION.

20. When were you Diagnosed that you are HIV infected……
21. When were you enrolled to the CTC known to be HIV infected? .....
22. When did you start using ART therapy……
23. Which type of ART therapy did you use……..
24. Have you ever been contacted with any drugs side effects since starts using ART?
    a) Yes
    b) No
25. Have you ever attached to psychosocial support groups
    a) Yes
    b) No
26. How often do you have a drink containing alcohol?
    A) Never take alcohol
    B) 2-4 times a month
    C) 2-3 times a week
    D) 4 or more times a week
    E) Everyday
    F) Don't know
27. Have you ever fill inability to take medication when you are away from home.
    a) Yes
    b) No
28. How many dose frequency do you take per day
    a) Single dose per day
    b) Twice per day
    c) More than twice day.
29. Have you ever encounter any reasons lead to fail take medication and cause non adherence.
    a) Forgot or busy
    b) Side effects
    c) Change in daily routine

d) Depression or illness
e) Lack of interest or drug holidays
f) Pills burden
g) No change in health status

30. Have you ever encounter problem satisfying food needs in past year
a) Never
b) Seldom
c) Sometimes
d) Often
e) Always

31. Usually how many meals do you take per day
a) Single meal
b) Two meals per day
c) Three or more meals per day

32. Have you ever failed to take medication because a drug requires food before taken?
a) Yes
b) No

33. What is the main reason for not taking ARVs?
A. Not eligible for treatment
B. Health care provider did not prescribe
C. Antiretroviral drugs are not available
D. I feel healthy/not sick
E. Cost of medications
F. Cost of transport
G. Religious reasons
H. Taking traditional medications
I. Not attending HIV clinic
J. Stigma/ keep HIV status secret
K. Other, (specify)
L. Don’t know
M. Refused
N. Don’t know

34. Have you ever experienced any kind of stigma?
    a) Yes
    b) No

if yes go to question 35

35. Where have you experienced a stigma?
    a) At the health facility by HCWs
    b) At the community
    c) At the family

36. What made you dissatisfaction with past experience of health care system leading to avoidance of coming to CTC?

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……...

Appendix 3. Ethical clearance