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HIV/AIDS Treatment Failure and its Determinant Factors Among First Line HAART Patients at Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia

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HIV/AIDS Treatment Failure and its Determinant Factors Among First Line HAART Patients at Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia

A thesis submitted to the department of Biology, College of science, Bahir Dar University in partial fulfillment of the requirements of the degree of master of science in Biology (Biomedical Sciences).

By

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APPROVAL SHEET

As members of the examining Board of the final MSc. open defense, we certify that we have read and evaluated the thesis prepared by: Bokretsion Gidey Brhane entitled: **HIV/AIDS Treatment Failure and its Determinant Factors Among First line HAART Patients at Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia** and recommended that it be accepted as fulfilling the thesis requirement for degree of MSc in Biology (Biomedical science).

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DECLARATION

I, the undersigned, declared that this MSc. thesis is my original work, has not been presented for a degree in any other university and that all sources of materials used for the thesis have been fully acknowledged.

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This thesis work has been submitted for examination with my approval as university advisor.

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ABSTRACT

Highly active antiretroviral therapy (HAART) played a critical role in the medical management of HIV infected individuals by restoring the immune function and minimizes HIV related outcomes. But treatment failure minimized these advantages and leads to an increment of morbidity and mortality with poor quality of life in all HIV patients. The aim of this study was to assess the prevalence of HIV/AIDS treatment failure and its determinants factors among patients on first line HAART at Felegehiwot Referral Hospital. Cross sectional study was conducted on 421 participants who had started first line HAART during August 01/ 2016 to September 30/2016. Data were collected from patients' chart starting from ART commencement (baseline data and other information) and face to face interview using structured questionnaire. CD4 T-cells from whole blood and viral load from separated plasma were analyzed according to protocols. The collected data were analyzed using SPSS packages version 20. Descriptive statistics, odds ratio, positive and negative predictive values, life table, receiver operating characteristics curves, bi-variate and multiple logistic regression were used to analysis. Independent associations were considered with $p<0.05$. Among the 421 participants enrolled, 243(57.7%) were females. The mean age was 30.2 years and the median months on HAART from initiation were 81 months. A total of 45(10.7%) participants were found to have treatment failure. The mean CD4 T-cells at initiation were 268.38cells/ml. The median time to detect virologic failure was 47 months. Sensitivity of immunologic failure in predicting virologic failure was 62.2%. Long duration on treatment, sub-optimal drug adherence (odds ratio: 9.55), conducting faith healing, immunologic failure, high medication dosage, ambulatory functional status at baseline and not feeling privacy during consultation and counseling were found to be significant predictors of treatment failure and positive odds ratio. Prevalence of treatment failure in Felegehiwot Referral Hospital needs high attention. Viral load determination in detection of treatment failure was earlier than CD4 T cells so immunologic failure in detecting virologic failure was acceptable. Adherence of treatment and other factors like duration on treatment was the predictor to treatment failure and should be assessed frequently.

Key words: treatment failure, first line HAART, HIV, determinant factors, Bahir Dar, Ethiopia.

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LIST OF ACRONYMS

3TC - *Lamivudine.*

AIDS-Acquired Immune deficiency syndrome

ANS -Amhara National State

ART-Antiretroviral therapy

AZT- *Zidovudine*

BDU-Bahir Dar University

CD4 -cluster of defereniation-4

cART- Combination antiretroviral therapy

D4T- *stavudine*

EFV-*efavirenz*

FACS- Fluorescent Activated cell sorter

HAART-highly active antiretroviral therapy

HIV-Human Immune deficiency

NRTI – Nucleoside reverse transcriptase inhibitor

NNRTI – Non-nucleoside reverse transcriptase inhibitor

NVP- *nevirapine*

TDF- *tenofovire*

WHO- World Health Organization

1. INTRODUCTION

1.1.Background and Justification

Although there is no curative therapy for HIV/AIDS, the advent of highly active antiretroviral therapy (HAART) played a critical role in the clinical management of HIV infected individuals by restoring the immune function, preventing morbidity and mortality, improving quality of life, and preventing the transmission of the virus to other uninfected individuals (Madec *et al.* 2013).

As of December 2011, over 8 million people infected with HIV were receiving antiretroviral therapy (ART) in low- and middle income countries which represents a 26-fold increase since 2005 (Hong *et al*., 2013; Hassan *et al*., 2014). Due to HIV's error-prone replication, high mutation rate and viral recombination, development of some HIV drug resistance (HIVDR) is inevitable, even with appropriate ART prescribing and adherence (Kebede and Wabe, 2012; Kassa *et al*., 2013; WHO, 2013; Lindsey *et al*., 2014). HIVDR has significant human and financial implications: it limits treatment options. Moreover, the second-line ART regimens involve more long-term toxicity and 4 to 8 times annual cost compared to first-line regimens (Mata-Marín *et al*., 2015). As the number of people on treatment increases, the emergence of meaningful population-level HIVDR becomes a greater risk which has the potential to undermine the dramatic gains that ART programs have had in reducing the morbidity and mortality of HIV-infected people in resource-limited settings (Luft *et al.,* 2011).

Despite the rapid scaling up of ART and its positive outcomes in adults, as of 2012 only 30% of HIV infected children (≤14 years) eligible for ART were receiving it. Moreover, the limited access of paediatric regimens, the challenges of paediatric ART adherence and the likelihood of

HIV drug resistance development raise great public health concern about treatment failure and drug resistance in children and even in adults receiving ART (Mulu *et al*., 2014).

In Ethiopia, ART service began in August 2003 with payment and free ART was launched in January 2005 (Shimelis *et al*., 2015).

Studies in East Africa have shown a high prevalence of immunologic failure ranging from 8% to 38% among clients on first-line HAART (Ahoua *et al*., 2009; Melsew *et al*., 2013; Kapesa *et al*., 2014), and furthermore, the magnitude increases as the time of follow-up increases. The immunological failure rate in Ethiopia a study conducted in Deberemarkos Hospital was found to be high (Melsew *et al.*, 2013). Conversely, the virologic failure rate in Ethiopia conducted in Gondar University Hospital showed that 4.1% was found to be low (Ayalew *et al*., 2016). The timing and accuracy of identifying treatment failure in resource-limited settings are fundamental but challenging (Yirdaw and Hattingh 2015). Delayed detection of treatment failure may increase drug toxicity, may lead to the accumulation of drug resistance associated mutations (further limiting treatment options), and may result in increased morbidity and mortality(WHO, 2013).

Monitoring of ART program factors known to be associated with the emergence of treatment failure for the purpose of improving programmatic functioning, may minimize the emergence of preventable HIVDR, especially at ART sites where viral load is not routinely available (Hong *et al.*, 2013; Kassa *et al.*, 2013; Wube *et al.*, 2013; Lindsey *et al.*, 2014). Viral load testing is required to predict the treatment failure of HIV in settings where inappropriate prescribing practices, treatment interruptions due to suboptimal patient adherence, poor patient retention on ART, or late initiation or when stock-outs occur. These factors have been shown to be associated with the development of HIV treatment failure (Jima *et al.*, 2013; Kassa *et al.*, 2013; Lindsey *et*

al., 2014; Mata-Marín *et al.,* 2015) thus, their monitoring may alert national ART program planners to issues which may be adjusted to minimize the treatment failure.

Moreover, there is a need of national baseline data on the level of treatment failure which will aid the third target of 90-90-90 (90% of all people live with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy and 90% of all people received antiretroviral therapy will have viral suppression) ambitious plan to help end the AIDS epidemic by 2020 (UNAIDS, 2014) to assist on the national treatment program by providing objective evidence. Moreover; there is a limited data regarding the treatment failure and factors increasing the treatment failure in first line HAART and in consequence, early and/or lately switch to second line HAART can happen with high expense of drug and toxic increments and more to uncontrolled drug resistance. Therefore, this study assessed the prevalence of HIV/AIDS treatment failure and its determinant factors among first line HAART patients in Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia.

1.2. Significance

This particular study was necessitated primarily because of concerns about treatment outcomes and patients' behavior of adhering to therapy which ultimately impacts on such outcomes like treatment failure and acquired drug resistance. Very few patients among the needy are started on second line ART regimens in Ethiopia (Bacha *et al.*, 2012)..

Now virologic failure has increased in human immunodeficiency virus (HIV) infection even in the era of Antiretroviral Therapy (ART). Virologic failure has emerged as significant problem for drug resistance and mortality on HIV positive patient and has been neglected in sub-Saharan African countries like the one in Ethiopia (Shimelis *et al*., 2015).

As far as our knowledge is concerned, there is research gap about treatment failure in this particular study area. Understanding of HIV/AIDS treatment failure and its determinant factors among patients who are on first line treatment would help for better clinical management of HIV patients who are on ART and late or immature switch to second line drug regimen.

The findings in this study would be used in alleviating ART adherence problem related with virological failure, in prioritizing resources and ensuring patient safety. Moreover, the findings could be used for designing or planning preventive interventions in the study area. Furthermore, the base line information generated in this particular study as reference for researches of similar kind in other parts of our country. The outcome of this study would also contribute to filling the existing gaps in current literatures on treatment failure and risk factors in Ethiopia.

1.3. Objectives

1.3.1. General objective

The general objective of this study was to:

- Assess the prevalence of HIV/AIDS treatment failure and its determinant factors among patients on first line highly active antiretroviral therapy (HAART) at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia.

1.3.2. Specific objectives

The specific objectives of this study were to:

- Determine the prevalence of HIV/AIDS treatment failure among patients on first line HAART at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia
- Estimate the mean time in months after treatment initiation when failure begins to occur at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia
- Evaluate clinical and immunological definitions of HIV/AIDS treatment failure as predictors of virologic treatment failure among patients on first line HAART at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia
- Assess determinant factors of HIV/AIDS treatment failure among patients on first line HAART at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia

2. LITERATURE REVIEW

2.1. Goals and Benefits of HAART

The efficacy of HAART in the suppression of plasma HIV-1 RNA to undetectable levels has been documented in clinical trials, however, the virological and immunological success rates reported from such trials may not be generalizable to the whole population of HIV-1 infected patients (Deeks and Volberding , 1997).

The primary goal of HAARTs are maximal and sustained suppression of viral replication, restoration of immunologic function, reduction of HIV related morbidity and mortality, improvement of quality of life and prolong survival, because of such use ART has become an integral part of the continuum of HIV care (Davies *et al*., 2012; Shimelis *et al.,* 2015).

The goals of offering cART to patients are many and include: maximal and durable suppression of viral replication and viral load reduction: these results in restoration and preservation of immunologic function (WHO, 2013; UNAIDS-WHO 2013; Yirdaw and Hattingh, 2015). Ultimately there is reduction of HIV-related morbidity and mortality. This also leads to significant improvement and prolongation of life which is also qualitative (UNAIDS, 2014). Another goal of therapy is to prevent or reduce mother-to-child transmission of HIV**.** As maternal viral burden reduces as a result of efficacy of antiretroviral medicines the possibility of in uterus transmission to the fetus is considerably reduced (Sebunya *et al.*, 2013). One of the consequences of maximal and durable suppression of viral replication is the prevention of mutation and emergence of resistant viral strains**.**

2.2. Mechanism of HIV mutation

As HIV replicates, mutations in the HIV genome develop due to errors in the transcription of RNA to DNA by the viral enzyme reverse transcriptase (John *et al.*, 2016) . When these errors are introduced into viral genes, a mutation may result. If the mutation occurs in one of the HIV proteins that is a target of an antiretroviral drug, the result may be decreased susceptibility or resistance to that drug, and lack of inhibition of viral replication by that drug. All progeny virions that are produced from a cell harboring mutant, resistant virus contain the same mutation or set of mutations. Approximately one mutation is introduced into the virus genome with each cycle of viral replication because HIV replicates at such a high rate, roughly one to 10 billion viral particles are produced daily (John *et al.*, 2016). Virtually all possible mutations in the HIV genome are generated within a patient on a daily basis. In this way, all HIV patients, including those naïve to therapy, harbor diverse population of viruses with differing susceptibilities to the currently available antiretroviral drugs. Because of the incidence of treatment failure, there is now a strong advocacy for resistance testing where resources will permit even before treatment initiation (John *et al.*, 2016).

2.3. Recommended ART drugs for HIV/AIDS patients

Research into the treatment of HIV infection has resulted in the development of five antiretroviral (ARV) drug classes another system of classification looks at six classes of antiretroviral medicines (WHO, 2013).

1. Nucleoside/Nucleotide Reverse Transcriptase inhibitors (NRTIs): *Abacavir*, *Didanosine*, *Emtricitabine*, *Lamivudine*, *Stavudine*, *Tenofovir* and *Zidovudine*; these are phosphorylated intracellularly and then inhibit the viral reverse transcriptase enzyme by acting as false substrate. 2. *Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs): Delavirdine*, *Efavirenz* and; these

inhibit the reverse transcriptase enzyme by binding to its active site. They do not require prior phosphorylation and can act on cell-free virions as well as infected cells. 3. Protease Inhibitors: *Amprenavir, Atazanavir, Fosamprenavir, Indinavir, Lopinavir/ ritonavir Nelfinavir, Ritonavir, Saquinavir and Tipranavir*. These bind to the active site of the HIV-1 protease enzyme preventing the maturation of the newly produced virions so that they remain noninfectious.

4. Entry Inhibitors: There are two subclasses, namely a) fusion inhibitors and b) chemokine coreceptor inhibitors. An example of fusion inhibitor is *Enfuvirtide* while *Maraviroc* belongs to the Chemokine Co-receptor inhibitor subclass. The target of action of these is the attachment/ entry stage in the HIV replication cycle. The linear 36-amino acid synthetic peptide inhibits fusion of the cellular viral membranes. 5. Integrase Inhibitor: an example is *raltegravir*

Triple regimens are accepted

Two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one Non-nucleoside Reverse Transcriptase Inhibitor (NNRTIs) or two NRTIs and one Protease inhibitor (PI) are used. In addition to the general principles, specific drug combinations are also recommended below and described as first line drugs (WHO, 2013).

Specific first line regimen recommended in Ethiopia [Ethiopian-Guideline, 2014]*: [Stavudine+Lamivudine] + Nevirapine , [Stavudine + Lamivudine] + Efavirenz , [Zidovudine + Lamivudine] + Nevirapine, [Zidovudine + Lamivudine] + Efavirenz , [Tenofovire₊ Lamivudine] + Efavirenz* and *[Tenofovire₊ Lamivudine] + Nevirapine.*

2.4. Eligibility of HAART in Ethiopia

ART in Ethiopia consists of generic low cost fixed-dose combination (FDC) of two NRTI and one NNRTI with first line regimens of *lamivudine* (3TC) as backbone combined with *stavudine*

(d4T) near to exit due to resistance or *zidovudine* (AZT), or *Tenofovire* (TDF) and either (NVP) or *efavirenz* (EFV). For anemic patients d4T substitutes AZT and for tuberculosis patients treated with *rifampicin* NVP replaces EFV (Assefa and Hussein, 2014; Ethiopian-Guideline, 2014; Mulu *et al.*, 2014).

2.5. Antiretroviral Therapy in Ethiopia

The scale up of free ART services has been one of the greatest achievements of the HIV program response over the last decade. ART program services have expanded on a large scale and have substantially decreased AIDS deaths and possibly contributed to the decline in HIV incidence since 2005. The number of facilities providing ART services has expanded in both health centers and hospitals, enabling the enrolment of hundreds of thousands of AIDS patients free of charge. The number of health facilities providing ART reached 913 in 2012/13, mainly public facilities (Federal Democratic republic of Ethiopia, 2014)

By the end of June 2013, the number of people ever enrolled in chronic care reached 728,874 while the number ever started ART was 439,301 and 317,443 were currently receiving ART. Only 70.3% of individuals who ever started ART were currently on treatment indicating challenges in patients‘ retention (Federal Democratic republic of Ethiopia, 2014).

In December 2013, Ethiopia adopted the new WHO integrated guidelines for treatment, in which adults with CD4 below 500 for ART initiation, all pregnant women and all TB patients independent of CD4 count are eligible for treatment. ART monitoring as planed also to be by using routine viral load monitoring starting from six month on ART in a yearly manner (Federal Democratic republic of Ethiopia, 2014).

Ethiopia has now reached a symbolic milestone for curbing the spread of the epidemic, where the number of newly started clients on ART (on average 58,000 adults each year) has surpassed the number of new infections in adults > 15 years (Federal Democratic republic of Ethiopia, 2014)

However, patient loss to follow-up and ensuring adherence to ART regimens remain major challenges of the ART program especially in some of the regions, as well as the inadequate capacity of some regions in the maintenance of laboratory machines (Federal Democratic republic of Ethiopia, 2014). One of the successes of the large scale free ART program has been its equal access by both men and women. When ART was first introduced in Ethiopia; women had substantially lower access to treatment services (Federal Democratic republic of Ethiopia, 2014).

Ethiopia adopted the 2013 WHO guideline to implement routine viral load monitoring (WHO 2013); moreover, the country is planning to achieve the 2020 ambitious plan an ambitious treatment target to help end the AIDS epidemic 90-90-90 program (UNAIDS-Ethiopia., 2014).

2.6. Associated Risk Factors to Treatment Failure

A study conducted in Ethiopia assessed the median time of treatment failure and associated risk factors to treatment failure. A total of 14 (4.1%) patients were found to have treatment failure. The median duration of treatment failure from initiation of treatment was 17.5 months (8–36 months). Poor adherence to treatment and low baseline CD4 cell count were found to be significant predictors of treatment failure (Ayalew *et al*., 2016). A similar study with high treatment failure rate was reported in Nigeria. The rate of treatment failure among the children was 18.8%. Previous antiretroviral drugs (ARV) exposure for treatment, not receiving cotrimoxazole prophylaxis before commencement of ART and having severe immune suppression at HIV diagnosis were the factors independently associated with treatment failure.

Children with previous ARV exposure for treatment were 4 times more likely to fail treatment compared to those without previous exposure (AOR=4.20 (1.93-9.15); p <0.001). Children who did not receive cotrimoxazole prophylaxis were twice more likely to develop treatment failure compared to those who did (AOR=2.26 (1.06-4.79); p=0.03) and children with severe immune suppression at HIV diagnosis were twice more likely to develop treatment failure compared to those without severe immune suppression (Ebonyi *et al*., 2014).

A cross-sectional study was reported in Costal Kenya, Of the 232 eligible participants on ART over a median duration of 13.9 months and virologic failure was 57 (24.6%). Younger age (15–34 vs. ≥35 years: and unsatisfactory adherence (<95% vs. ≥95%) were strong correlates of virologic failure (Hassan *et al.,* 2014). In Uganda a long term virologic failure was conducted, 526 adults and 250 children were analyzed on first-line ART regimens (Mayanja-kizza *et al*. 2007). Children were almost twice as likely to have viral failure compared with adults (26%vs. 14%; P = 0.0001). In adults, the sole independent predictor of viral failure was treatment with *stavudine* (d4T)/*lamivudine* (3TC)/ (NVP) versus *zidovudine* (ZDV)/3TC/efavirenz (EFV) (odds ratio [OR] = 2.59, 95% confidence interval [CI]: 1.20 to 5.59). In children, independent predictors of viral failure included male gender (OR = 2.44, 95% CI: 1.20 to 4.93), baseline CD4%, (OR = 2.69, 95% CI: 1.28 to 5.63), and treatment with d4T/3TC/NVP versus ZDV/3TC/EFV (OR =2.46, 95% CI: 1.23 to 4.90).

Another systematic review was conducted in 18 studies the poor sensitivity ranged from 16.8 to 54.9%, specificity from 82.9 to 95.5%, PPV from 15.0 to 38.8%, and NPV from 90.9 to 98.6%. Seven studies assessed clinical criteria to predict viral load of more than 50 to more than 1000 copies/ml; the sensitivity was 11.0%, specificity 90.5%, PPV 44.9%, and NPV 90.2%. Seven studies assessed clinical or immunologic criteria defining virologic failure as viral load of more

than 50 to more than 1000 copies/ml; their sensitivity was 26.6%, specificity 85.9%, PPV 49.4%, and NPV 91.1%. Four studies assessed immunologic criteria in children; three defined Virologic failure as viral load at least 5000 copies/ml and one as viral load at least 400 copies/ml. The sensitivity ranged from 4.5 to 6.3%, specificity from 97.7 to 99.3%, PPV from 20.0 to 54.9%, and NPV from 85.5 to 91.8% (Rutherford *et al.,* 2014).

A retrospective study had indicated low value of immunological predictors as virological failures in Nigeria. A total of 9690 patients were included in the analysis (median follow-up, 33.2 months). A total of 1225 patients experienced failure by both immunologic and virologic criteria, 872 by virologic criteria only, and 1897 by immunologic criteria only. The sensitivity of CD4 cell criteria to detect viral failure was 58%, specificity was 75%, and the positive-predictive value was 39%. For patients with both virologic and immunologic failure, VL criteria identified failure significantly earlier than CD4 cell criteria (median, 10.4 vs 15.6 months; P, .0001). Because of the low sensitivity of immunologic criteria, a substantial number of failures are missed, potentially resulting in accumulation of resistance mutations. In addition, specificity and predictive values are low, which may result in large numbers of unnecessary ART switches. Monitoring solely by immunologic criteria may result in increased costs because of excess switches to more expensive ART and development of drug resistant virus (Rawizza *et al.,* 2011).

A study in Kampala, Uganda had been studied. Of 701 children, 240 (34%) failed on first line ART. The overall median time (IQR) to first line ART failure was 26.4 months. The factors associated with treatment failure were poor adherence, exposure to single dose (sdNVP) and a NVP containing regimen. One in three children on first-line ART was likely to develop virological treatment failure after the first 24 months of therapy. Poor adherence to ART, a NVP

based first-line regimen, prior exposure to sdNVP were associated with treatment failure (Sebunya *et al.,* 2013).

In south Africa a cross-sectional description of 465 patients had concordantly match the virological and immunological failures with 19% both immunological and virological failed and significantly associated with cumulative adherence of < 95% to drug refill visits after a median of 15 months on HAART. Analyzing the risk of virologic failure over time using Kaplan Meier survival analysis, the virologic failure rate was 23% up until month 99. There was a significant difference in time to virologic failure between patients with complete vs. incomplete adherence. By month 12 on ART, the failure rate was similar but by month 48, the difference in failure rates had reached statistical significance between the groups, 19% vs. 37% respectively (El-Khatib *et al*., 2011).

A study in Ethiopia, consecutive HIV-1 infected adults and children who have been receiving ART virological suppression and immunological recovery was observed in 82% adults and in 87% children on a median time of 24 months on ART. Median CD4+ T cell count has increased from baseline 124 to 266 and 345 to 998 cells/mm3 in adults and children respectively after 12 months of ART. This indicates that despite limited resources in the setting virological efficacy can be sustained for a substantial length of time and also enhance immunological recovery irrespective of age. However, the presence of drug resistance mutations and low level viraemia among clinically asymptomatic patients highlights the need for virological monitoring *(*Mulu *et al.*, 2014).

Research to assess treatment outcomes in HIV management is performed differently, depending on the setting, methodology, endpoints, resources and the level of expertise among other things.

But since the goal of HAART is to achieve maximal viral suppression, virological failure will remain one of the most important treatment outcomes to monitor especially in resource limited settings where viral resistance testing remain largely/routinely unavailable. It is also pertinent that events surrounding this important outcome are well understood.

3. MATERIALS AND METHODS

3.1. Study Area and Period

This study was conducted at Felegehiwot Referral Hospital in Bahir Dar town, northwest Ethiopia and data collection period was from August 01 to September 30/ 2016. Bahir Dar town has two public hospitals, five public health center, three higher private clinics and one Regional laboratory. The town is located approximately 578 km north-northwest of Addis Ababa, having longitude of 11°36′N 37°23′E and an elevation of about 1,800 meters (5,906 feet) above sea level. According to the 2015 Bureau of finance and Economics Development of Amhara National Regional State, the population of Bahir Dar including rural kebeles is 297,749 of which 141,245 are males and 156,504 are females (BOFED, 2015).

Felegehiwot Referral Hospital gives service to over 5,000,000 people. Its ART sections give a service to over 17,856 patients ever enrolled on ART. Out of these, by the end of 2014 the patients on first line HAART were 10098 patients (Federal Democratic republic of Ethiopia, 2014).

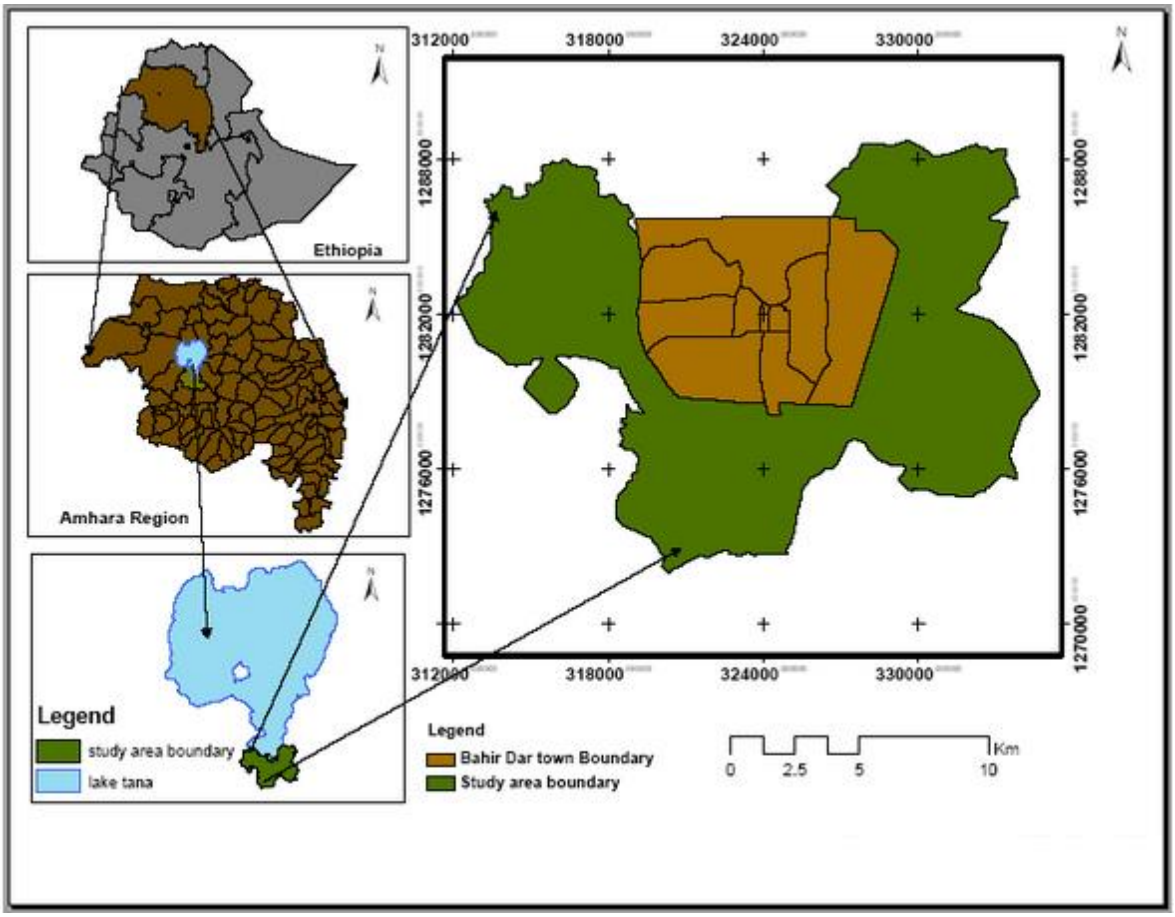

Figure 1: Map of Bahir Dar town: source: (Ebistu and Minale, 2013)

3.2. Study design

- Hospital based cross sectional study was conducted at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia.

3.3. Source population

- All HIV/AIDS patients who were enrolled at first line HAART follow up in Felegehiwot Referral Hospital.

3.4. Study population

- All HIV/AIDS patients who were enrolled in HAART program, who met the inclusion criteria and present during study period to get service from ART section of Bahir Dar Felegehiwot Referral Hospital, northwest Ethiopia.

3.5.Inclusion and Exclusion criteria

Inclusion criteria

- All HIV/AIDS patients who were enrolled in first line HAART and who attended the clinic for routine visits, and followed the treatment for at least six months during the study period were included.

Exclusion criteria

- Patients on second line treatment and on first line treatment followed the HAART for less than six months and those patients having Acute Febrile Illness (AFIs) which can increase viral load falsely were excluded from this study.

3.6. Sampling technique and Sample Size

Systematic random sampling technique was used to select 421 participants from ART follow up who took first line HAART for at least six months.

The sample size is calculated using Single population proportion by considering the following assumptions; $\mathbf{n=z^2p\ (1\text{-}p)/w^2}$ (Naing *et al*., 2006; Arya and Antonisamy, 2017)] **n** = required minimum sample size from single population= 384, W= estimated error =0.05; **P** = population proportion in problem (estimated prevalence) = 0.5, $\mathbf{Z\ \alpha/_2}$= 1.96 standard normal value at 95% level of confidence, so, n=384+38 (10% contingency from loss of participant by any case) = 421 participants included in this study.

3.7. Socio-demographic and determinant factors assessment

Data were collected from patients' card starting from ART commencement (baseline data and other information) and face to face interview using structured questionnaire. The questionnaire was developed based on review of different literatures having different questions related to the determinant factors. The questionnaire was translated from English to Amharic language and finally to English.

3.8. Specimen Collection and laboratory investigation

Two experienced data collectors (one laboratory technician and one nurse) were involved in data collection and laboratory analysis of the samples.

Blood collection: Five millimeters venous blood with EDTA tube were collected for determining viral load and CD4 counts parameters based on standard procedure.

Determination of CD4 counts

To determine CD4+ T cells and CD4%, fifty micro litters of fresh whole blood was added to single reagent tube and processed according to the protocol set by Becton Dickinson Biosciences (BD, San Jose, California, USA). Results of CD4 counts were found from baseline (HAART initiation) to peak value (any time but peak CD4 value after HAART initiation before started declines) at registration book and current (at time of collection) result was done from fresh whole blood as the protocol specified above.

Determination of Viral Load

The whole blood containing EDTA anticoagulant was allowed to settle for 15 to 30 minutes and, then centrifuged at 3000-4000 rpm for 5 min and the plasma was separated from the cell within 6 hours and stored at -20^0C if the analysis was delayed. To determine viral copy/ml with a lower detection limit of 40 copies/ml, six hundred micro liter plasma was added to reagent tube and processed according to the procedure using a quantitative real time HIV-1 assay (by m2000sp and m2000rt Abbott, USA).

Data Quality

The validity of the questionnaires was assured by proper designing and also pre-testing the questionnaire in 5% of respondents other than those involved in actual study. Before commencing the actual data collection, training was given to the data collectors. Questionnaires were reviewed and checked by the supervisors and principal investigators. The necessary feedback was offered to data collectors in the next morning.

Specimen and Reagents quality

The quality of the specimens was checked every day before going to analysis according to Amhara Public Health Research institute's laboratory standard operating procedures. Reagents

and instruments were checked periodically for accuracy and reproducibility following manufacturer instruction.

3.9. Data Processing and Analysis

Variables of the study

Dependent variable: Treatment failure/ virologic failure.

Independent variables: Patient medication Adherence, Socio-demographic variables (age, sex, marital status, occupational, and educational status), WHO clinical stages, CD4 count (baseline, peak value, current), ART regimen, Income, Change/substitute of treatment, Detection of tuberculosis during the course of therapy and Alcohol usage were assessed. Moreover, knowledge and perception on HIV and ART (knowledge and information on ART, Perception of treatment) service delivery environment distance from home to the clinic, quality of care, trust in health care (private consultancy) providers, pill burden concerns.

Data analyses

The data were cleaned, checked for completeness and entered in to EPI info version 3.5.1 and compiled and analyzed using SPSS packages version 20. Descriptive statistics, odds ratio (both crude odds ratio and adjusted odds ratio), Sensitivity, specificity, Positive predictive value, Negative predictive value, life table and ROC curves were used in the analysis. Percentage, means, medians, standard deviations and ranges were used to describe findings. The data were also analyzed using univariate and multivariate logistic regression and to determine the effect of various factors on virologic failure.

The cumulative prevalence of first-line ART failure was ascertained from the proportion of participants with viral load ≥1000 copies/ml at one point for virologic failure. Similarly, immunologic and clinical treatment failures were defined according to WHO (WHO, 2013);

CD4+ T cell count below the baseline or persistent CD4+ T-cell levels below 100 cells/mm3 for immunologic failure. Logistic regression analysis was done to determine the extent to which the risk factors are associated with HAART treatment failure. All socio demographic and clinical characteristics (variables) were subjected to uni-variate analysis for calculating Crude Odds Ratio (COR). To identify the independent explanatory variable (s) of the dependent variable, factors with $p< 0.25$ at univariate analysis were selected and included in multivariate analysis (Lutalo *et al.*, 2016). The model was then built by dropping the most insignificant factor one at a time in step-wise manner and the factor (s) that appeared in the final model with $p<0.05$ was taken to be the factor (s) that independently associated with treatment failure.

3.10. Ethical consideration

Institutional Ethical clearance was obtained from Bahir Dar University Ethics Review Committee. Formal letter of cooperation wrote to Felegehiwot Referral Hospital. Each respondent was informed about the objective of the study and findings of the study for improving health of those attending ART section. Written consent and assent were obtained from each study participant. Involvement in the study was endorsed only after written consent is obtained. Any person who was not willing to participate in the study was not forced to participate. They also informed that all data obtained from study participant kept confidential by using codes instead of any personal identifiers. Abnormal results were communicated with physician to let the patients get additional treatment.

3.11. Operational Definition

1. **Adherence** means adhering to a treatment regimen; for the patient it means, taking all the pills and doses in accordance with the manner prescribed by the doctor, and also means maintaining certain lifestyle patterns (e.g. stop smoking and alcohol intake), attending follow-up appointments, collecting all prescriptions, maintaining a healthy diet and other therapeutic behaviors like exercise (WHO, 2013).
2. **Antiretroviral drugs** (ARVs) are drugs that interfere with the replication of retroviruses like HIV and are used to stop the progression of HIV disease by reducing the viral load and thereby allowing some recovery of the immune system (WHO, 2013).
3. **HAART**- Highly Active Antiretroviral Treatment also called combination antiretroviral treatment (c-ART) involves the use of at least three different antiretroviral drugs with a backbone of two NRTIs and either a NNRTI or a PI, to fully suppress viral replication during HIV infection (WHO, 2013).
4. **Immunological response** is an increase in CD4 cell count by at least 50 – 120 cells/ml during the first 3 months on HAART and correlates with the duration of viral suppression (WHO, 2013).
5. **First line ART regimen is** the first combination of antiretroviral drugs a patient can be given as treatment for HIV infection**.**
6. **Treatment failure** can be classified as **clinical failure** (new or recurrent AIDS-defining illnesses after at least 6 months of ART), **immunologic failure** (fall to baseline CD4 level or 50% fall of CD4 cell count from treatment peak or levels of CD4 cells persistently less than 100 cells/μl) and **Virologic failure** is a sustained increase in viral load of more than

1000 copies/ml at least 3 months apart in a patient on HAART for at least 6 months (WHO, 2013).

7. **Virologic response (Optimal viral suppression)** is described as the decrease in viral load less than 40 copies/ml by 24 weeks or a sustained suppression of viral load of less than 40 copies/ml (UNAIDS-WHO, 2013).
8. **Viraemia** refers to a detectable plasma viral load irrespective of whether or not one is on HAART (WHO, 2013).

4. RESULTS

4.1. Socio-demographic characteristics

From a total of 421 study participants, 292 were adults and 129 were children with a mean age of 30.2 with standard deviation of 16 (39.65±9.68 adults and 9.8±3.7 children years). In the adult age category, 117(40.1%) of them were in age category of 31-40 years and 80 (27.4%) were in 41-50 years, and the rest 262 (89.7 %) were in 18-50 years. In children age category, 27(20.9%) of them were in the age category of 1-5 years, 31(24%) were in 6-10 years, and the rest 71(55.1%) were in 11-17 years (Table1). Sex wise, 73 (56.6%) of the children were females whereas 170 (58.2%) of the adults were females. Regarding the educational level of participants, 95 (32%) of them completed primary school, 72 (24.7%) completed college or university and the rest 62 (21.2%) had no formal education. Regarding the educational level of children, 34(26.4%) did not attend any formal education, 80(62%) attended primary school and the rest 15(11.6%) completed their high school studies.

Regarding monthly income of adult participants, about 79 (27 %) had no regular income whereas 221(52.5 %) had a monthly income ranging from781-3500 Birr. Similarly, the monthly income of the guardians were 76(58.9%) in the range of 781-2250 ETB where as 18(14%) in <780 and 36(17.1%) in the range of 2551-10000. Occupational wise, looking at the adults 88(30.1%) were governmental employees and 41(14%) were unemployed. Out of the total adults, 151 (51.7%) were married. The other 141 (48.3%) were single, divorced or widowed. The majority of study participants (adults: 273 (93.5%) and children 118(91.5%) were urban dwellers of Bahir dar town and its nearby towns (Table 1).

Table 1: Socio-demographic characteristics (N=421)

Variable		Adults	Children
Age	18-30	65(22.5%)	
	31-40	117(40.1%)	N/A
Adults	41-50	80(27.4%)	
	51-80	30(10.3%)	
Children	1-5		27(20.9%)
	6-10	N/A	31(24%)
	11-17		71(55.1%)
Gender			
Female		170(58.2%)	73(56.6%)
Male		122(41.8%)	56(43.4%)
Residence			
Urban		273(93.5%)	118(91.5%)
Rural		19(6.5%)	11(8.5%)
Marital status			
Single		30(10.3%)	
Married		151(51.7%)	N/A
Divorced		59(20.2%)	
Widowed		52(17.8%)	
Educational Status			
Not formal/not in school		62(21.2%)	34(26.4%)
Primary school		95(32.5%)	80(62%)
Secondary		63(21.6%)	15(11.6%)
Tertiary		72(24.7%)	N/A
Occupational status(Adults)			
Gov. Employee		88(30.1%)	
Merchant		47(16.1%)	
Driver		8(2.7%)	N/A
House wife		35(12%)	
Unemployed		41(14%)	
Self employee		73(25%)	
Monthly Income (Birr)		Participant	Family income
Unknown		79(27.1%)	N/A
1-780		53(18.2%)	18(14%)
781-2250		81(27.7%)	76(58.9%)
2251-3500		46(15.8%)	18(14%)
3501-10,000		33(13.3%)	17(13.1%)

4.2. Baseline clinical and immunologic characteristics

The mean CD4 count at ART initiation was 268.38 cells/ µl (range 2–1321 cells/ µl). Majority of study participants, 284(67.5%) had suffered an AIDS defining illness (clinical status) i.e. WHO stages 3 and 4 conditions at the time of ART initiation. The proportion of patients who commenced ART after developing signs or symptoms suggestive of mild immunosuppression (WHO stage 2) was 81(19.2%). Only 56(13.3%) of participants commenced ART before developing HIV associated symptoms or signs i.e. WHO stage 1 (Table 2). During HAART commencement, 316 (75.1%) and 105(24.9%) were working and ambulatory by patient functional status. TB infection is the most dominant opportunistic disease in HIV/AIDS. Out of 421 participants, TB infection was confirmed in 129(30.6%) starting from HAART initiation (Table 2).

4.3. Types of ARV first line regimen during initiation

During treatment initiation, different types of first line (initial regimen) ART drugs were used as choice of treatment for HIV/AIDS patients. Having this point, d4T based regimen contained NNRTIs of both NVP (d4T/3TC/NVP) and EFV (d4T/3TC/EFV) were 115(27.3%) and 30(7.1%) respectively. Similarly, the AZT based regimen was highest into AZT/3TC/NVP and AZT/3TC/EFV 194(46.1%). On the other hand TDF based regimens consisted of TDF/3TC/EFV and TDF/3TC/NVP were 58(13.8%) and 24(5.7%) respectively (Table 2).

Regarding treatment regimen substitution, only 162 (38.5%) study participants received a substitution while they were on first line regimen whereas 259(61.5%) of them did not receive any substitutions (Table 2). Out of the total substitutions, AZT based substitution was 63(19.1%) followed by TDF 33(11.3%) and D4T 20 (3.1%). The reasons for substitution were toxicity/side effect, occurrence of TB infection, and pregnancy.

Table 2: Baseline clinical and immunologic characteristic (N= 421)

Variables	Category	Frequency (%)
Baseline first line HAART regimen	D4T/3TC/NVP	115(27.3%)
	D4T/3TC/EFV	30 (7.1%)
	AZT/3TC/NVP	140(33.3)
	AZT/3TC/EFV	54(12.8%)
	TDF/3TC/NVP	58(13.8%)
	TDF/3TC/EFV	24(5.7%)
First line HAART substitution	D4T/3TC/NVP	4(2.5%)
	D4T/3TC/EFV	16(9.9%)
	AZT/3TC/NVP	68(42.0%)
	AZT/3TC/EFV	38(23.4%)*
	TDF/3TC/NVP	15(9.2%)
	TDF/3TC/EFV	21(13.0%)
	Total	**162(100%)**
Baseline CD4 results	≤ 100	112(26.6%)
	101-350	216(51.3%)
	351-500	40(9.5%)
	≥501	53(12.6)
Baseline WHO stages	I	56(13.3%)
	II	81(19.2%)
	III	237(56.3%)
	IV	47(11.2%)
Baseline patient functional status	Ambulatory	105(24.9%)
	Working	316(75.1%)
TB history	Yes	129(30.6%)
	No	292(69.4%)

4.4. Prevalence Clinical, Immunologic and Virologic failures

Clinical failure

WHO stages I (no AIDS case) and II (mild AIDS case) were the most dominant clinical presentations 374 (88.8) participants. Forty seven (11.2%) of participants were at stage III. In the current study, stage 4 clinical presentations were not observed during the study time, this may be due to the study participants were from out patients (Table 3).

Immunologic failure

Quantitative restoration of CD4+ T cells is one of the principal evidences for immune recovery during HAART. Out of 421 study participants, 67(15.9%) encountered immunologic failure in which 40(16.5%) and 27(15.2%) were females and males respectively. Over time analysis of immunologic failure has shown that 28(42.8%) study participants encountered immunological failure within 6-48 months while 15(22.4%) and 24 (35.8%) of them encountered within 49-72 months and 73-158 months, respectively. Immunologic failure was independently associated with virologic failure (p-value < 0.05) (Table 3).

Virologic failure

During the study period, out of 421 study participants in first line HAART regimen, prevalence of virologic failure (≥1000 RNA copies per ml) was found to be 10.7% (45/421); 26 (10.7%) females and 19 (10.7%) males. Since the start of HAART, out of the total study participants, 23(51.1%) of them encountered virological failure within 6-48 months followed by 8(17.8%) of them within 49-72 months and 14(31.1%) within 73-158 months (Table 3).

Treatment failure

In detecting treatment failure in HAART, clinical, immunologic and virologic failures are important. Generally, the prevalence of treatment failures were 45(10.7%), 67(15.9%), and

47(11.2%) of them encountered virologic failure, immunologic failure, and clinical failure respectively. The mean of months on which they were on HAART was 75.7 months and the median time was 81.0 months with a standard deviation of 34.4 with a maximum of 156 months (13 years). The median time from HAART initiation to identification of treatment failure was 47 months for virologic failure and 63 months for immunologic failure. Moreover, the backbone of treatments which showed treatment failure of AZT/3CT/NVP and AZT/3CT/EFV was 25(55.6%) and TDF/3CT/NVP and TDF/3CT/EFV was 20(44.4%) (Table 3).

During study time, out of 421 participants, 261(62.0%) were following AZT based regimen while 138(32.8%) were following TDF based regimen. The rest 22 (5.2%) were following D4T based regimen were considered as current regimen. Viral suppression was assessed as of under lower detection limit (< 40 RNA copies/ ml) and the rate was 357(84.8%) (Table 3).

Table 3: Treatment failure after initiation of HAART in HIV/AIDS patients (N=421)

Variable	Categories	Frequency (%)
Presence of treatment failure	Yes	84(20%)
	No	337(80)
Clinical failure (WHO stages)	Yes	47(11.2%)
	No	374(88.8&)
Immunologic failure	Yes	67(15.9%)
	No	354(84.1%)
Virologic failure	Yes	45(10.7%)
	No	376(89.3%)
Treatment failure regimen backbone	AZT/3TC	25(55.6%)
	TDF/3TC	20(44.4%)
Months from ART initiation	6-48	23(51.1%)
	49-72	8(17.8%)
	73-158	14(31.1%)
First line HAART regimen	D4T/3TC/NVP	12(2.8%)
	D4T/3TC/EFV	10(2.4%)
	AZT/3TC/NVP	170(40.3%)
	AZT/3TC/EFV	91(21.6%)
	TDF/3TC/NVP	79(18.9%)
	TDF/3TC/EFV	59(14.0%)
Viral suppression	Yes	357(84.8%)
	No	64(15.2%)

4.5. Performance characteristics of clinical and immunologic failures in prediction of virologic failure

In this study, by ROC curve analysis the area under the curve (AUC) was 0.759 (95% CI: 0.672-0.847) (Figure 2). Immunologic failure had fair predictive values to virologic failure. Sensitivity of immunologic failure compared to the golden standard, virologic failure, was 62.2% whereas the specificity of immunologic failure was 89.6%. Positive predictive value (PPV) was 41.8% and Negative predictive value (NPV) was 95.2% (Table 4).

ROC curve analysis of clinical failure showed that the area under the curve was 0.484 (95% CI: 0.393-0.576). This area indicated that clinical failure was less predictive of the occurrence of virologic failure. The performance of clinical failure to identify treatment failure, sensitivity was 17.8%, specificity was 89.3%, positive predictive value was (17.0%) and negative predictive value was (90.1%) (Table 4).

Table 4: Performance characteristics of clinical and immunologic failures in predicting virologic failure

Criteria	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Clinical failure	17.8	89.3	17.0	90.1
Immunologic failure	62.2	89.6	41.8	95.2

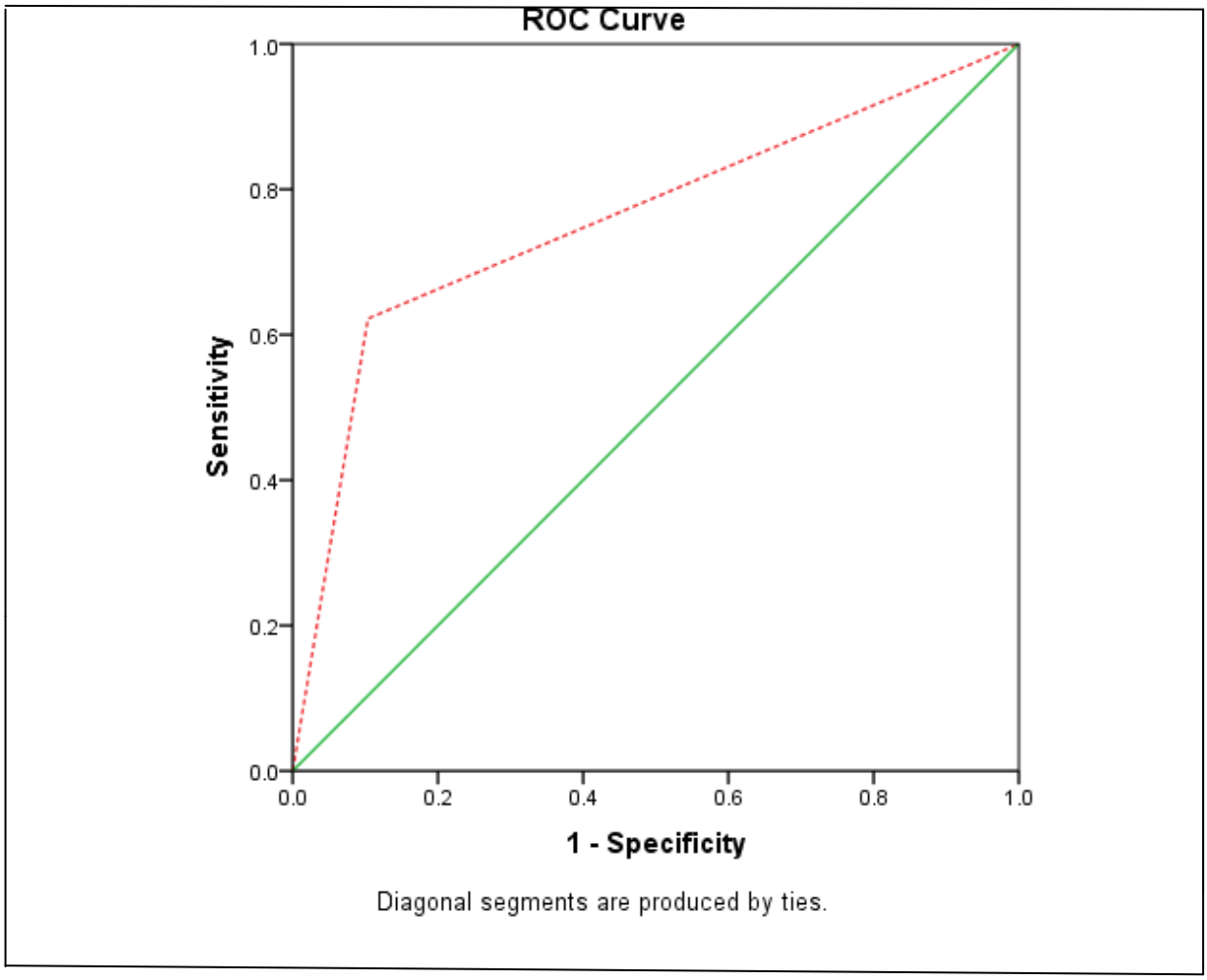

Figure 2: By Roc curve analysis performance of immunologic failure in predicting virologic failure in detection of treatment failure at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia, 2017

4.6. The time at which treatment failure began

The time to detection of treatment failure: stands for the time between ART initiation and detection of failure of first line ART (virologic failure and immunologic failure). In Kaplan Meier survival analysis, the time at which failure occurs is compared between immunologic and virologic monitoring methods by considering the entire 421 study participants. Out of 421 participants, 84(19.9%) showed both virologic failure and immunologic failure. Analysis of treatment failure criteria showed that viral load criterion was able to identify failure earlier (Median, 47.0 months; 95% CI: 18.08-75.91, $p<0.05$) than the criterion of CD4 T cells count to identify immunologic failure (Median, 63.0 months; 95% CI: 51.9-74.02) (Table 5) and more stated as the functional survival of the virologic and immunologic failures (Figure 3 and 4).

Table 5: Survival time to detect treatment failure after treatment initiation

Variables	Category	Mean	Median
Virologic failure	Yes	57.956 (46.331-69.580)	47.0 (18.081-75.919)
	No	77.819 (74.470-81.169)	82.0 (78.766-85.234)
Immunologic failure	Yes	59.791 (51.097-68.485)	63.0 (54.971-74.029)
	No	78.706 (75.243-82.169)	75.0 (78.141-85.859)

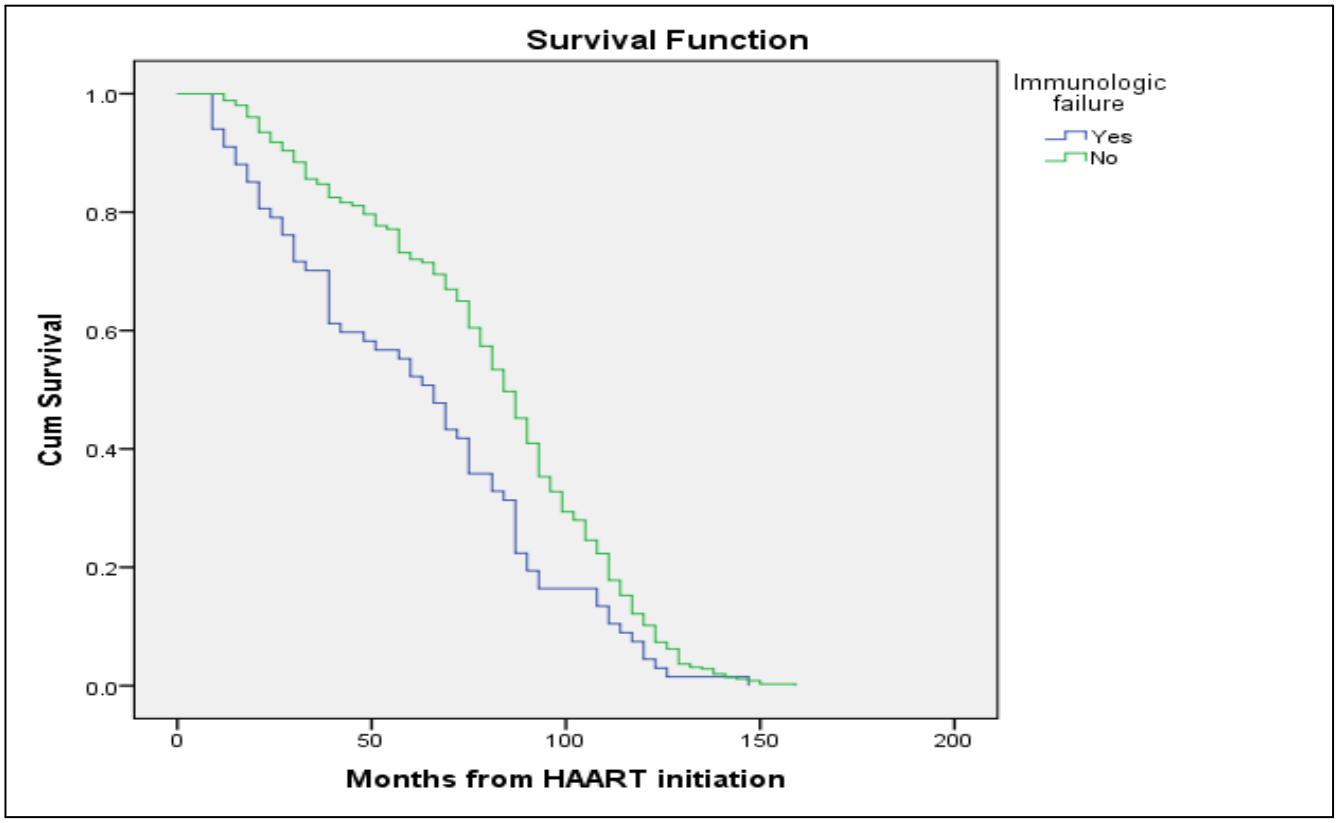

Figure 3: The time at which first line HAART immunologic failure began at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia, 2017

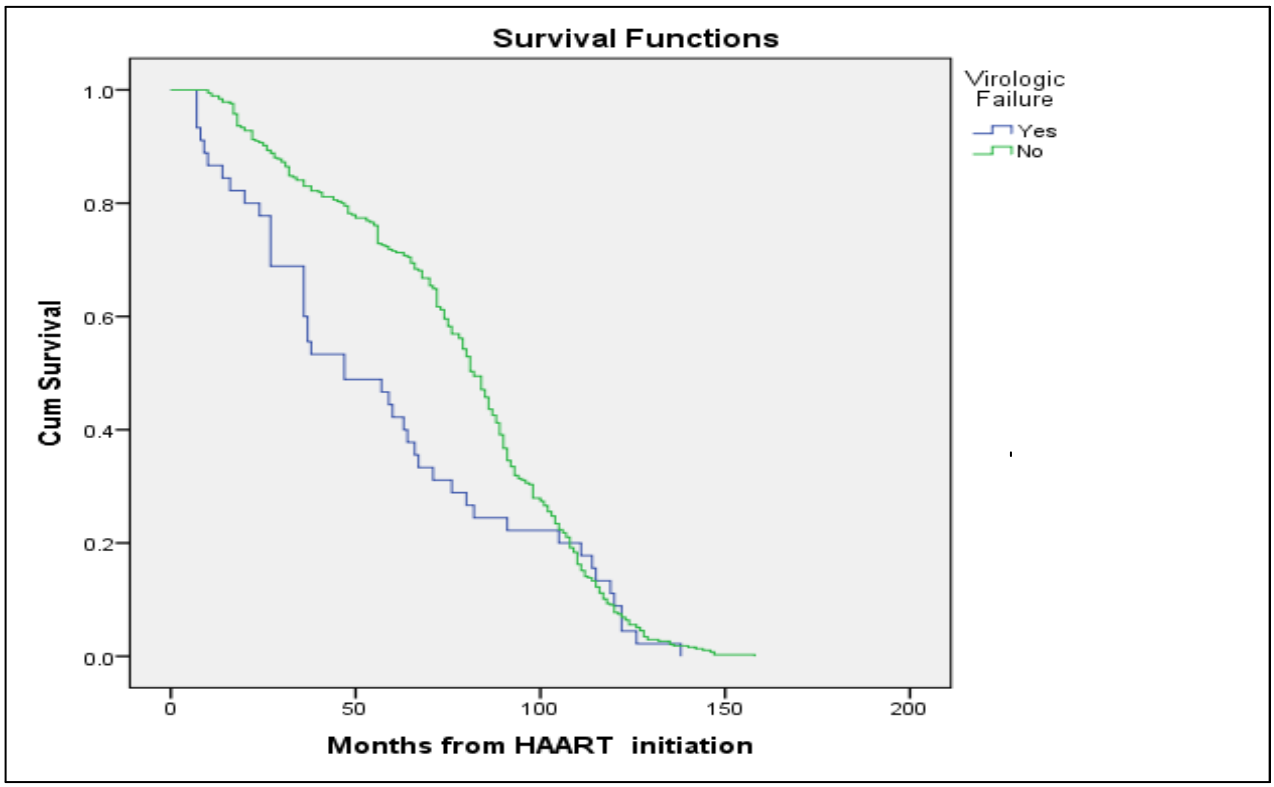

Figure 4: The time at which first line HAART virologic failure began at Felegehiwot Referral Hospital, Bahir Dar, northwest Ethiopia, 2017

4.7. Determinant factors of HIV/AIDS treatment failure among patients on first line HAART

4.7.1. Bi-variate logistic regression analysis

Using bi-variate logistic regression, association was assessed between age, gender, Residence educational status, income, medication dosage, distance, consultation privacy, faith heal, drug adherence, WHO stage baseline, TB history, CD4 baseline, immunologic failure, duration of treatment, baseline patient functional status, regimen substitutes, baseline regimen, 1st line current regimen with virological failure at various intervals. In this analysis, different criteria were checked like crude odds ratio and p-value for multiple logistic regression analysis consideration. Therefore, educational status, income, medication dosage, distance, consultation privacy, faith heal, drug adherence, TB history, CD4 baseline, immunologic failure, duration of treatment, baseline patient functional status and regimen substitutes were entered to analysis (table 6 and 7).

The bi-variate associations were observed without controlling the effect of other confounding factors it is very difficult to conclude whether the observed statistically significant association was because of the existing causal relationship between the given independent variables and the treatment failure. Since both the dependent and independent variable coded to dichotomous and multiple logistic regression analysis was used to confirm the independent associations.

Table 6: Bi-variate logistic regression analysis of socio demographic associated factors with virologic failure

Variables	Categories	All (n=421)	VF (n=45)	Odds Ratio (OR, 95% CI)	P-value
Gender	Female	243	26	1	1
	Male	178	19	0.998 (0.536-1.875)	0.993
Age group	Children	129	16	0.779 (0.407-1.49)	0.450
	Adult	292	29	1	1
Residence	Urban	391	43	1	1
	Rural	30	2	1.730 (0.399-7.517)	0.465
Educational status	No formal education	96	15	0.491 (0.18-1.336)	0.164
	primary	175	20	0.705 (0.271-1.834)	0.473
	secondary	78	4	1.682 (0.455-6.22)	0.436
	Tertiary	72	6	1	1
Distance from home to clinic	≤10 km	248	30	1	1
	>10 km	173	15	1.450 (0.755-2.784)	0.265
consultation of privacy	Yes	399	34	1	1
	No	22	11	6.435 (2.81-14.73)	0.000
Faith healing medicine	Yes	94	27	7.045 (3.67-13.54)	0.000
	No	327	18	1	1

Table 7: Bi-variate logistic regression analysis of clinical associated factors with virologic failure

Variables	Categories	All(n=421)	VF(n=45)	Odds Ratio (OR,95% CI)	P-value
CD4 value baseline	≤ 100	112	22	3.04 (1.61-5.711)	0.001
	>100	309	23	1	1
Duration of ART treatment	6-48	105	23	1	1
	49-72	70	8	2.174 (0.911-5.186)	0.080
	73-158	246	14	4.648 (2.284-9.459)	0.001
Drug adherence	<95	74	25	8.342 (4.311-16.143)	0.001
	≥95	347	20	1	1
Drug substitutes	Yes	157	22	1.708 (0.917-3.178)	0.091
	No	264	23	1	1
Medication dosage	1-2	333	24	1	1
	3-5	88	21	4.035 (2.123-7.672)	0.001
Types of drugs	AZT based	283	25	1.749 (0.934-3.275)	0.081
	TDF based	138	20	1	1
Functional status	Ambulatory	105	26	5.145 (2.709-9.771)	0.001
	Working	316	19	1	1
TB ever	Yes	129	21	2.171 (1.160-4.064)	0.015
	No	292	24	1	1
Immunologic failure	Yes	67	28	14.232 (7.154-28.313)	0.001
	No	354	17	1	1

4.7.2. Multiple logistic regression analyses

Multiple logistic regression analyses there were statistical significant associations between the following factors and treatment failure: duration of treatment, immunologic failure, baseline patient functional status, medication dosage, consultation privacy, conducting faith heal, adherence to ART during study period, and treatment failure. However, there were no statistical significance associations ($p > 0.05$) between educational status, distance from home to clinic, TB history, CD4 baseline, regimen substitutes, gender, age and that of treatment failure.

In this study, long duration (months) on treatment was independent predictor to treatment failure. Long duration on treatment (73-158 months) was strong risk factor for treatment failure/virologic failure as the patients with long time on first line HAART treatment (adjusted odds ratio= 5.797, 95% CI: 1.661-20.232)) were 5.79 times more likely to have treatment failure when compared to patients with short duration on treatment (6-48 months) (Table 9).

Adherence was defined as optimal and sub-optimal (based on pill count and self report at each visit) when it was ≥ 95% and < 95% respectively. Sub-optimal drug adherence (< 95%) was independent associated risk factor of treatment failure as patients with sub-optimal adherence patients (adjusted odds ratio=9.553, 95% CI: (3.488-26.164)) were > 9 times more likely risk of treatment failure when compared to optimal adherence (≥95%) patients. Similarly when compared to the patients who conducted faith healing (adjusted odds ratio=8.124, 95% CI: 3.075-21-465) and these patients who did not conduct *faith healing*/ *holy water* were 8.12 times more risky to develop and associated with higher risk of treatment failure. Religious beliefs and practice the so known 'holy water' leads to patient poor adherence from HAART care. Majority

of patients who conduct healing holy water sessions are persuading patients to discontinue HAART treatment because they think as they are healed (Table 9).

Based on WHO criteria, immunologic failure was assessed and checked whether had associated with treatment /virologic failure and found to be significant predictor of the presence of treatment failure/virologic failure. Immunologic failure was high risk factor for treatment/virologic failure as the patients with immunologic failure (adjusted odds ratio= 8.630, 95% CI: 3.321-22.424) were 8.6 times more likely to have treatment/virologic failure when compared to the patients who had not failed immunologically. Similarly high pill burden/medication dosage (≥ 3 tablets a day) was high risk to develop treatment failure when compared to patients who took one or two tablet daily. High pill burden/medication dose was associated risk factor for developing treatment failure as the patients were used high medication dose (Adjusted odds ratio=3.827,95% CI:1.360-10.773) were 3.82 times more risky when compared to the patients who used low medication dose (one or two a day) (Table 9).

Ambulatory baseline patient functional status was found significant risk factor to treatment failure. Ambulatory functional status was high risk to develop treatment failure, as the patients with ambulatory functional status (adjusted odds ratio = 2.972, 95% CI: 1.185-7.455) were 2.97 times more likely to have treatment failure when compared to the patients who had working functional status. Moreover, not feeling privacy during consultation and counseling of HIV treatment was shown independent risk factor to treatment failure. Not feeling privacy during consultation and counseling was high risk to increase treatment failure as the patients who did not feel privacy during consultation and counseling (adjusted odds ratio= 4.855, 95% CI: 1.499-15.792) were 4.85 times more likely to have treatment failure than the patients who had felt privacy during consultation and counseling on treatment failure (Table 8)

Table 8: Multiple logistic regression analysis of socio demographic associated factors with virologic failure

Variables	Categories	All (n=421)	VF (n=45)	Crude Odds Ratio (COR, 95% CI)	P-value	Adjusted Odds Ratio AOR(95% CI)	P-value
Gender	Female	243	26	1	1	1	1
	Male	178	19	0.998 (0.536-1.875)	0.993	1.332 (0.504-3.520)	0.563
Age group	Children	129	16	0.779 (0.407-1.49)	0.450	2.161 (0.423-11.031)	0.354
	Adult	292	29	1	1	1	1
Educational status	No formal education	96	15	0.491 (0.18-1.336)	0.164	0.299 (0.056-1.594)	0.157
	primary	175	20	0.705 (0.271-1.834)	0.473	0.592 (0.141-2.488)	0.474
	secondary	78	4	1.682 (0.455-6.22)	0.436	1.846 (0.325-10.473)	0.489
	Tertiary	72	6	1	1	1	1
consultation of privacy	Yes	399	34	1	1	1	1
	No	22	11	6.435 (2.81-14.73)	0.001	4.865 (1.499-15.792)	0.008*
Functional status	Ambulatory	105	26	3.190 (1.246-8.165)	0.001	2.972 (1.185-7.455)	0.020*
	Working	316	19	1	1	1	1

Table 9: Multiple logistic regression analysis of clinical associated factors of virologic failure)

Variables	Categories	All (n=421)	VF (n=45)	Crude Odds Ratio (COR, 95% CI)	P-value	Adjusted Odds Ratio AOR(95% CI)	P-value
CD4 value baseline	≤ 100	112	22	3.04 (1.61-5.711)	0.001	0.514 (0.127-2.080)	0.351
	>100	309	23	1	1	1	1
Duration of ART treatment	6-48	105	23	1	1	1	1
	49-72	70	8	2.174 (0.911-5.186)	0.080	2.240 (0.597-8.402)	0.101
	73-158	246	14	4.648 (2.284-9.459)	0.001	5.797 (1.661-20.232)	0.006*
Faith heal medicine	Yes	94	27	7.045 (3.67-13.54)	0.001	8.124 (3.075-21-465)	0.001*
	No	327	18	1	1	1	1
Drug adherence	<95	74	25	8.342 (4.311-16.143)	0.001	9.553 (3.488-26.164)	0.001*
	≥95	347	20	1	1	1	1
ARV regimen substitutes	Yes	157	22	1.708 (0.917-3.178)	0.091	0.548 (0.193-1.566)	0.259
	No	264	23	1	1	1	1
Medication dosage	1-2	333	24	1	1	1	1
	3-5	88	21	4.035 (2.123-7.672)	0.001	3.827 (1.360-10.773)	0.016*
TB ever	Yes	129	21	2.171 (1.160-4.064))	0.015	1.697 (0.601-4.786)	0.318
	No	292	24	1	1	1	1
Immunologic failure	Yes	67	28	14.232 (7.154-28.313)	0.001	8.630 (3.321-22.424)	0.001*
	No	354	17	1	1	1	1

5. DISCUSSION

As HAART continues to be scaled up in Ethiopia, with more Primary Health Care (PHC) facilities providing ART services, increasingly more efforts and resources need to be directed at ensuring that patients who continue to enroll at these facilities receive quality care to optimize their health. This particular study was designed to identify treatment outcomes, mainly virologic failure, as a way to assess programme performance at ART facility.

Virologic failure is a golden standard for detecting treatment failure in HAART. Prevalence of treatment failure was 10.7% (45/421) among the study participants. The mean and median time on treatment was 75.7 and 81 months which signifies high suppression rate 84.8% (viral load below detection limit). There is a possibility of improving the suppression rate near to 100% by providing an efficient early HAART service such as letting patients to commence ARV early and ensuring adherence of patients to treatment. Similar study conducted in Uganda reported prevalence of treatment failure 9.9% (Reynolds *et al*., 2009) which is comparable to the result of the present study. Compared to other studies, this study revealed a lower prevalence of treatment failure than the one reported (23.2%) from Cameron (Meriki *et al*., 2014) and also from costal Kenya (24%) (Hassan *et al*., 2014). The probable reason for lower failure in the present study might be that the great majority 391(92.9%) of participants being urban dwellers which gives them an advantage over the rural dwellers in getting information from a number of media and easily accessible to health facilities. It is also possible that the existence of nearby ART clinic which is at a distance of 10 km, on average, might give the chance the urban dwellers to frequently visit the clinic for further information. The present study, however, showed higher treatment failure rate compared with 4.1% which was reported from Gondar (Ayalew *et al*.,

2016). The higher prevalence in the present study might be because of poor adherence and high duration on treatment that could possibly increase treatment failure.

In treatment failure, viral load criteria identified failure significantly earlier (median, 47.0 months; $p<0.001$) than did CD4 count criteria (median, 63.0 months). In this survival analysis, time to failure is compared between immunologic and virologic monitoring methods among the entire 421 participants. The present study indicated a higher time to failure (47 months) compared to a median time of 15 months which was reported from South Africa (El-Khatib *et al*., 2011), 24 months from Cameron (Meriki *et al*., 2014), 24 months from Gondar, Ethiopia (Zeleke, 2016), 19.7 months from Addis Ababa, Ethiopia (Bacha *et al*., 2012). Interestingly, as duration on HAART increased, drug failure increased especially in long duration of 73-158 months treatment. This is, however, independently associated with virologic failure. A similar study conducted in Cameron showed long time duration of treatment to be one of determinant factors for treatment failure (Zoufaly *et al*., 2013) and this particular factor, long duration on treatment, for example, for above 60 months among patients in Gondar, Ethiopia, was found to be an independent predictor for an increased risk of HIV treatment failure (Zeleke, 2016).

By ROC curve analysis, performance of immunologic failure was evaluated against good predictive capacity of virologic failure. Accordingly sensitivity of 62.2%, specificity of 89.6%, positive predictive value of 41.8%, and negative predictive value of 95.2% were found. These values are higher than those values 23% (sensitivity), 90% (specificity), 21% (positive predictive value), and 91% (negative predictive value) reported from Uganda (Reynolds *et al.*, 2010). Similarly, the values of the present study are higher than the values (sensitivity of 34%; specificity of 94%; positive predictive value of 75%; and negative predictive value of 71%) reported in another study conducted in Tanzania (Mgelea *et al.,* 2014*).* Reason for fair predicting

value ROC analysis and its higher values other studies is probably due to longer median time to failure of HAART with good adherence of patients.

Using multivariate logistic regression, there was an association between treatment failure and the following factors: long duration of treatment (73-158 months, $p< 0.05$), immunologic failure, baseline functional status, high medication dosage, not feeling privacy during consultation, faith heal and sub-optimal adherence to ART during study period. However, there was no statistical significant association ($p> 0.05$) between treatment failure and the following factors: educational status, distance to clinic, TB history, CD4 baseline, base line regimen, and regimen substitutes.

Before patients commence HAART, it is essential that they should be adequately prepared for this life-long drug therapy. ART treatment necessitates a change in life style and social habits. Poor patient treatment follow up may lead to poor drug adherence by patients, increasing the likelihood of treatment failure. A similar study in South Africa has shown that incomplete adherence as one of the risk factors for virologic failure (El-Khatib *et al*., 2011). Similarly, a study in Kenya has shown that unsatisfactory adherence to have strong correlation with virologic failure (Hassan *et al*., 2014). In Gondar, Ethiopia, poor adherence during follow up has been shown to be associated with treatment failure (Zeleke, 2016).

This study indicated that faith heal, mostly known by community as "*Holy Water*" was found to be associated factor with treatment failure. Some people go to the place where this holy water is available and they greatly believe in its healing power. Alternative medicine or faith heal is one of the major factors that makes patients to less adhere to HAART. Although, there is no study that depicted the statistical association of treatment failure with holy water, some studies, however, have indicated an evidence of positive outcomes of faith healing involving holy water

and spiritual aspects that mentally benefit the chronic patients (Kloos *et al.*, 2013). On the contrary, the very existence of high prevalence of holy water in Debrebirhan, Ethiopia, has been implicated as hindrance (not taking medicines as a spiritual fear to holy water) to HAART, (Kebede and Shewangizaw, 2015).

Functional status (ambulatory/bedridden) at baseline is associated factor to treatment failure and in line with study done in Addis Ababa, Ethiopia (Yimer and Yalew, 2015; Haile *et al*., 2016).
In the present study, high medication dosage currently taken by patients (Jean-Jacques *et al*., 2004), consultation privacy and immunologic failures were the factors that were associated with treatment failure/virologic failure.

Limitation: Viral load was done only once at cut off value >1000 RNA copies/ml due to budget constraint. Consequently, there may be missed classification of HIV treatment failure as of not repeated after three months. Acquired drug resistance was not done due to the lack of reagents and available instruments.

6. CONCLUSION

The present study reported moderate prevalence of treatment failure and needs attention. Viral load testing is best in early detection of treatment failure than CD4 T cells count and should be used in a routine ART laboratory. Both clinical and immunologic failures did not complement each other to predict virologic failure. Nevertheless, immunologic failure in the present study was found to be fair in predicting virologic failure compared to other studies. Furthermore, the present study showed that long duration of treatment, immunologic failure, baseline functional status, high medication dosage, not feeling privacy during consultation and counseling, conducting faith heal, and sub-optimal adherence to be determinant factors of treatment failure/virologic failure.

7. RECOMMENDATIONS

Based on the findings of the present study, the following are recommended.

- ✓ In resource poor settings, CD4 counting is acceptable and affordable and it should be supportive and be conducted in parallel with viral load testing.
- ✓ After confirming the HIV positive status, the onset of treatment should quick and the patients should be followed to detect any treatment failure to improve HAART service.
- ✓ Duration of time on first line HAART should be checked frequently to protect unnecessary drugs (failed treatment) and early switch to second line HAART is important.
- ✓ Adherence and other risk factors should be monitored regularly as per the HIV treatment guidelines.
- ✓ Avoiding delays in ART initiation, reinforcing adherence interventions, developing and widely implementing affordable HIV-1 RNA monitoring is important.

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9. ANNEXES

Informed Consent and Information Sheet for participants (For Adults English version)

Informed consent

I am ....., working at Bahir Dar Felegehiwot referral hospital. I am going to give you information and invite you to participate in this research. Please feel free to ask for further clarification in any issues that you may not understand. You can withdraw from the study at any time and failure to participate in this study will not affect the services you receive at this hospital.

Entitled: HIV/AIDS treatment failure and its determinant factors among first line HAART patients at Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia

This study is being conducted by **Bokretsion Gidey Brhane** as part of **MSc** graduate in **Biology department at Bahir Dar University** and it will be explore the determinant factors for first line treatment failure among patients on first line HAART and also recommend possible intervention to improve ART management. You are being to participate, in this study because you are on ART medication at this hospital which has been selected as part of this study.

If you accept to participate, this interview which will take about 15 minutes, 10 ml venous blood will collect, information about your health status will collect form your patient profile. Your direct benefit from this study is that, your viral load level will be determined and attached with your medical record to assist your follow up. You will be provided with proper adherence and support which will be complimented this study and will assist you to support your treatment outcome.

There is no known risk in participating in this study, though you might feel that your time has been inconvenienced. Any information that you provide to us will be kept confidential. Information collected from you will be stored securely and only the researchers will access to it. Also we will not use your name on the questionnaire; we will use an identification number that will be assigned to you.

Consent agreement

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Signature of Participant _____ Signature of data collector _____

Date_____ Date _____

Informed Consent and Information Sheet for participants (For Children English version)

I am ....., working at Bahir Dar Felegehiwot referral hospital. I am going to give you information and invite you to have your child participate in this research. Please feel free to ask for further clarification in any issue that you may not understand. You can withdraw your child from the study at any time and failure to participate in this study will not affect the services you and/or your child receives at this hospital.

Entitled: "HIV/AIDS treatment failure and its determinant factors among first line HAART patients at Felegehiwot Referral Hospital, Bahir Dar, Northwest Ethiopia"

This study is being conducted by **Bokretsion Gidey Brhane** as part of **MSc** graduate in **Biology department at Bahir Dar University** and it will be explore the determinant factors for first line treatment failure among patients on first line HAART and also recommend possible intervention to improve ART management. Your child is being to participate, in this study because your child on ART medication at this hospital which has been selected as study site. Your decision to have your child participate in this study is entirely voluntary.

If you accept to participate, this interview which will take about 15 minutes, 10 ml of venous blood will be collected, information can be collected from his/her patient profile. Your child direct benefit from this study is that, his/her viral load level will be determined and attached with his/her medical record to assist his/her follows up. Your child will be provided with proper adherence and support which will be complimented this study and will assist him/her to support his/her treatment outcome.

There is no known risk in participating in this study, the risk associated with this study could be some discomfort related with minors' needle brick injury pain and in a rare occasion a hematoma may be developed blood collection, though you might feel that your time has been

inconvenienced. Any information that you provide to us will be kept confidential. I Also we will not use your name on the questionnaire and sample tubes.

Assent agreement

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I assent voluntarily to my child as a participant in this research.

Signature of Participant _____ Signature of data collector _____

Date_____ Date _____

Questionnaires (English version)

Study no/…….Patient card……..Unique ART…….Date of HAART Eligibility …….

Status of respondent (circle the answer): ☐ **A**=Adult (≥18 years old); ☐ **B**=Children (<18 years)

Part I - Socio Demographics characteristics

1. Participant's residence? ☐ 1=Urban ☐ 2=Rural
2. Gender; ☐ 1=Female ☐ 2=Male
3. Age (year for adult, Year + month for children); _____
4. Educational status? ☐ 1= Illiterate ☐ 2=Primary school education ☐ 3=secondary/high school education ☐ 4= college or university graduate
5. Marital status participant; ☐ 1=single ☐ 2=married ☐ 3=Divorced ☐ 4=Widowed
6. Occupation of the participant; ☐ 1=Government employee ☐ 2= Merchant ☐ 3=Housewife ☐ 5=Student ☐ 6=Unemployed ☐ 7=other, specify_____
7. Average monthly income in birr;_____
8. Distance from your residence to the HIV clinic in kilo meter? ☐ 1= ≤10km ☐ 2= >10km

Part II- Associated risk factors to HAART medication

9. How many medications did you take at a time/daily? ☐ 1= One ☐ 2= two ☐ 3= three ☐ 4=four ☐ 5= other specify_____
10. Currently in use types of first line regimen (ARV)?

☐ **1a**=d4t/3TC/NVP; ☐ **1b**=d4t/3TC/EFV; ☐ **1c**=AZT/3TC/NVP; ☐ **1d**=AZT/3TC/EFV; ☐ **1e**=TDF/3TC/EFV; ☐ **1f**=TDF/3TC/NVP

11. WHO clinical stage currently (during interview)? ☐ 1= stage I ☐ 2=stage II ☐ 3= stage III ☐ 4= stage IV

Do you have privacy during consultation and counseling? ☐ 1= Yes ☐ 2= No

Part III: Behavior and knowledge related

12. In the last one month have you used alcohol? ☐ 1=Yes ☐ 2= No

13. Do you use alternative medicine (faith healing)? ☐ 1=Yes ☐ 2= No

14. Is it possible to cure HIV/AIDS? ☐ 1=Yes ☐ 2= No

15. Is it necessary to use condoms if both partners are HIV positive? ☐ 1=Yes ☐ 2=No

Part four: Information's collected from patient cards

16. When did you start HAART medication in months and years? _____/_____

17. Baseline patient functional status? ☐ 1= working ☐ 2= ambulatory ☐ 3= bedridden

18. WHO clinical stage during initiation? ☐ 1= stage I ☐ 2=stage II ☐ 3= stage III ☐ 4= stage IV

19. How is ART drug adherence (self report)? ☐ 1= good ☐ 2= fair ☐ 3 =poor

20. Baseline first line regiment type (during initiation)? ☐ **1a**=d4t/3TC/NVP; ☐ **1b**=d4t/3TC/EFV; ☐ **1c**=AZT/3TC/NVP; ☐ **1d**=AZT/3TC/EFV; ☐ **1e**=TDF/3TC/EFV; ☐ **1f**=TDF/3TC/NVP

21. TB history from initiation? ☐ 1= Yes ☐ 2 = No

22. Is there baseline regimen substitutes? ☐ 1=Yes ☐ 2= No

23. Reason for drug change/substitutes from baseline regimen? ☐ 1= side effect/toxicity ☐ 2= availability ☐ 3= pregnancy ☐ 4= TB infection

24. Baseline CD4 results while HAART initiation? _____cells/ml?

25. CD4 peak value after HAART initiation? _____cells/ml?

Part IV: laboratory results

26. CD4 counts of T cells_____cells/ml

27. Viral load results_____RNA copies/ml

Thank you!

Informed Consent and Information Sheet for participants (Adults Amharic version)

ባህርዳር ዩኒቨርሲቲ በድህረ-ምረቃ ክፍል

ባዮሎጂ ፕሮግራም

የመረጃ ቅፅ

ይህ መጠይቅ በባህር ዳር ፈለገ ሂወት ሪፈራል ሆስፒታሎች የኤ.አር.ቲ.ክትትል ከሚያገኙ ኤች.አይ.ቪ. በደማቸው ውስጥ ከሚገኝባቸው ሰዎች በቫይረስ መጠን በመለካት፤ቫይራል ሎድ እና ኢሚኖሎጂክ መረጃ በመጠቀም የመድሃኒት መላማመድ አለ/የለም ለማጥናት የተዘጋጀ ነው፡፡

የጥናቱ ርእሰ፡ “የአንደኛ ደረጃ አማራጭ የኤች.አይ.ቪ. መድሐኒት የመቋቋም ወይም የመላመድ አቅም እና ተያያዥ ሁኔታዎችን ለማወቅ የሚረዳ ጥናት ለማከሄድ የተዘጋጀ የጥናቱ ተሳታፊዎች የመረጃና የስምምነት ቅፅ”

<u>መግቢያ</u>

ጤና ይስጥልኝ: ስሜ ---------- ይባላል፡፡ የምሠራው በባህርዳር ሪፈራል ሆስፒታል ኤ.አር.ቲ ክፍል ውስጥ ነው፡፡ወደ ዚህ የመጣሁበት ምክንያት ኤች.አይ.ቪ. በደማቸው ውስጥ ከሚገኝባቸው ሰዎች የቫይረሱ መጠን በመለካት የመድሀኒት መላመድ አለ/የለም ለማጥናት የተዘጋጀ ነው፡ ጥናቱን የሚያካሂዱት በባህርዳር ዩኒቨርስቲ በድህረ-ምረቃ ክፍል ባዮሎጂ ፕሮግራም የሁለተኛ ዓመት የማስተርስ ተማሪ የሆኑት አቶ በክረፅዮን ግደይ ብርሃነ ናቸው፡፡ በአሁኑ ሠዓት በደማቸው ውስጥ ኤች.አይ.ቪ. ከሚገኝባቸው ሰዎች አላሰፈላጊ መድሃኒት በመቀየር በሽታውና መድሃኒቱን በመላማመድ በጤና ላይ ከፍተኛ የሆነ ጉዳት እያደረሰ ይገኛል፡፡ የዚህ ጥናት ዋና ዓላማ በባህርዳር ፈለገ ሂወት ሪፈራል ሆስፒታል የኤ.አር.ቲ. ክትትል ከሚያገኙ ኤች.አይ.ቪ. በደማቸው ከሚገኝባቸው ሰዎች መድሃነት መላመድ አለ/የለም እና ስርጭቱ ምን ያህክል ነው፡፡ በጥናቱ ጊዜ የአንተን/ቺን የደም ናሙና እንሰበስባለን፡፡

ስለዚህ የተወሰኑ ጥያቄዎች አሉን፡፡ ከዚህ የሚገኘው ማንኛውም መረጃ በሚስጥር ይጠበቃል፡፡ ለዚህም ሲባል የእርስዎ ሥም እና አድራሻ አይጻፍም፡፡

በዚህ ጥናት መሳተፍዎ እና መተባበርዎ መድሃኒቱን የሚደርሰውን ጉዳትና ሞት ለመቀነስ ከፍተኛ አስተዋጽዖ አለው፡፡ ለመመለስ ፈቃደኛ ያልሆኑትን ማንኛውንም ጥያቄ አልመልስም ማለት ይችላሉ፡፡ በማነኛውም ሰዓት የጥያቄ እና መልሱ ንሂደት ማቋረጥ ይችላሉ፡፡ ነገርግን ቀደም ሲል እንደተገለጸው እርስዎ የሚሰጡት እውነተኛ ምላሽ በጤናዎ ለሚከሰቱ በሽታ የሚታመሙትንና የሚሞቱትን ቁጥር ለመቀነስ የሚደረገውን እንቅስቃሴ በከፍተኛ ሁኔታ ያግዛል፡፡

በመጨረሻም ከአንተ/ቺየምን ሰበስበው መረጃ ከስምህ/ሽ ጋር አይያያዝም ስምህን/ሽን እና አድራሻህ/ሽ እንደማይጠቀስና ለማንም አካል ተላልፎ እንደማይሰጥ ልናረጋግጥልህ/ሽእን ወዳለን::

የዚህ ጥናት ዓላማ ተነቦልኝ (አንብቤው) እ ናዓላማው ገብቶኝ በጥናቱ ለመሣተፍ

1. ፈቃደኛ ሆኛለሁ (ቃለ-መጠይቁን መቀጠል ይቻላል)_____
2. ፈቃደኛ አይደለሁም (ቃለ-መጠይቁን ያቁሙ)_____

<u>የስምምነት ማረጋገጫ ቅጽ</u>

ይህንን ግንዛቤ ውስጥ በማስገባት በጥናቱ ላይ እንድትሳተፍ/ፊ በክብር እንጠይቃለን፡፡ እኔ ከዚህ በታች ፊርማዬን የተቀመጠው በጥናቱ በፍቃደኝነት እሳተፋለሁ ስል የሚከተሉትን ግንዛቤ ውስጥ በማስገባት ነው::

1. የጥናቱ ዓላማ
2. በጥናቱ የሚካተቱ ጥያቄዎችንና የጥናቱ አስፈላጊነት

በሚገባኝ ቋንቋ ስለተገለጸልኝና ስለተብራራልኝ በጥናቱ ለመሳተፍ በፊርማዬ አረጋግጣለሁ::

የተሳታፊ ፊርማ _____ የመረጃ ሰብሳቢ ፊርማ _____

ቀን_____ ቀን_____

Informed Consent and Information Sheet for participants (Children Amharic version)

ባህርዳር ዩኒቨርሲቲ በድህረ-ምረቃ ክፍል

ባዮሎጂ ፕሮግራም

<u>የመረጃ ቅፅ</u>

ይህ መጠይቅ በባህር ዳር ፈለገ ሂወት ሪፈራል ሆስፒታሎች የኤ.አር.ቲ.ክትትል ከሚያገኙ ኤች.አይ.ቪ. በደማቸው ውስጥ ከሚገኝባቸው ሰዎች በቫይረስ መጠን በመለካት፤ቫይራል ሎድ እና ኢሚኖሎጂክ መረጃ በመጠቀም የመድሃኒት መላማመድ አለ/የለም ለማጥናት የተዘጋጀ ነዉ፡፡

የጥናቱ ርእሰ፡ “የአንደኛ ደረጃ አማራጭ የኤች.አይ.ቪ. መድሐኒት የመቋቋም ወይም የመላመድ አቅም እና ተያያዥ ሁኔታዎችን” ለማወቅ የሚረዳ ጥናት ለማከሄድ የተዘጋጀ የጥናቱ ተሳታፊዎች የመረጃና የስምምነት ቅፅ

<u>*መግቢያ*</u>

ጤና ይስጥልኝ: ስሜ ---------- ይባላል፡፡ የምሠራው በባህርዳር ሪፈራል ሆስፒታል ኤ.አር.ቲ ክፍል ውስጥ ነው፡፡ወደ ዚህ የመጣሁበት ምክንያት ኤች.አይ.ቪ. በደማቸው ውስጥ ከሚገኝባቸው ሰዎች የቫይረሱ መጠን በመለካት የመድሀኒት መላመድ አለ/የለም ለማጥናት የተዘጋጀነዉ፡ ጥናቱን የሚያካሂዱት በባህርዳር ዩኒቨርስቲ በድህረ-ምረቃ ክፍል ባዮሎጂ ፕሮግራም የሁለተኛ ዓመት የማስተርስ ተማሪ የሆኑት አቶ በክረፅዮን ግደይ ብርሃነ ናቸው፡፡ በአሁኑ ሠዓት በደማቸው ውስጥ ኤች.አይ.ቪ.ከሚገኝባቸ ውሰዎች አላሰፈላጊ መድሃኒት በመቀየር በሽታው መድሃኒቱን በመላማመድ በጤና ላይ ከፍተኛ የሆነ ጉዳት እያደረሰ ይገኛል፡፡ የዚህ ጥናት ዋና ዓላማ በባህርዳር ፈለገ ሂወት ሪፈራል ሆስፒታል የኤ.አር.ቲ. ክትትል ከሚያገኙ ኤች.አይ.ቪ. በደማቸው ከሚገኝባቸው ሰዎች መድሃነት መላመድ አለ/የለም እና ስርጭቱ ምን ያህክል ነው፡፡ በጥናቱ ጊዜ የልጅዎ የደም ናሙና እንሰበስባለን በተጨማሪም ከካርድ ክፍል መረጃ እንሰበስባለን፡፡ ስለዚህ የተወሰኑ ጥያቄዎች አሉን፡፡ ከዚህ የሚገኘው ማንኛውም መረጃ በሚስጥር ይጠበቃል፡፡ ለዚህም ሲባል የልጅዎ ሥም እና አድራሻ አይጻፍም፡፡በዚህ ጥናት የልጅዎ ተሳተፎ እና መተባበርዎ በመድሃኒቱን ችግር የሚደርሰውን ጉዳትና

ሞት ለመቀነስ ከፍተኛ አስተዋጽዖ አለው፡፡ ለመመለስ ፈቃደኛ ያልሆኑትን ማንኛውንም ጥያቄ አልመልስም ማለት ይችላሉ፡፡ በማነኛውም ሰዓት የጥያቄ እና መልሱን ሂደት ማቋረጥ ይችላሉ፡፡ ነገርግን ቀደም ሲል እንደተገለጸው እርስዎ/ልጅዎ የሚሰጡት እውነተኛ ምላሽ በህፃናት ለሚከሰቱ በሽታ የሚታመሙትንና የሚሞቱትን ቁጥር ለመቀነስ የሚደረገውን እንቅስቃሴ በከፍተኛ ሁኔታ ያግዛል፡፡በመጨረሻም ከልጅዎ የሚሰበስበው መረጃ ለማንም አካል ተላልፎ እንደማይሰጥ ልናረጋግጥልህ/ሽ እንወዳለን::

የዚህ ጥናት ዓላማ ተነቦልኝ (አንብቤው) እና ዓላማው ገብቶኝ በጥናቱ ለመሣተፍ

1. ፈቃደኛ ሆኛለሁ (ቃለ-መጠይቁን መቀጠል ይቻላል)
2. ፈቃደኛ አይደለሁም (ቃለ-መጠይቁን ያቁሙ)

<u>የስምምነት ማረጋገጫ ቅጽ</u>

ይህንን ግንዛቤ ውስጥ በማስገባት በጥናቱ ላይ እንድትሳተፍ/ፊ በክብር እንጠይቃለን፡፡ እኔ ከዚህ በታች ፊርማዬን የተቀመጠው በጥናቱ በፍቃደኝነት እሳተፋለሁ ስል የሚከተሉትን ግንዛቤ ውስጥ በማስገባት ነው::1. የጥናቱ ዓላማ፤ 2. በጥናቱ የሚካተቱ ጥያቄዎችንና የጥናቱ አስፈላጊነት በሚገባኝ ቋንቋ ስለተገለጸልኝና ስለተብራራልኝ በጥናቱ ለመሳተፍ በፊርማዬ አረጋግጣለሁ::

የተሳታፊ ፊርማ _____ የመረጃ ሰብሳቢ ፊርማ_____

ቀን_____ ቀን_____

Questionnaires (Amharic version)

የጥያቄው መለያ ቁጥር_____

መጠይቁ የተካሄደበት ቀን___/____/2008ዓ.ም

የጠያቂው ሥምና ፊርማ_____ _____

የተቆጣጣሪ ስምና ፊርማ_____ _____

ክፍል አንድ: መሰረታዊ መረጃዎችን የተመለከቱ ጥያቄዎች

መመሪያ: **የሚከተሉትን ጥያቄዎች በጥንቃቄ ካነበቡ በኋላ እያንዳንዱ በተሰጠው የመልስ መስጫ ቦታ መልሱን ይሙሉ::**

1. **የሚኖሩበት ቦታ? ☐1. ከተማ ☐2. ገጠር**
2. **ጾታ? ☐1. ሴት ☐2. ወንድ**
3. **ዕድሜህ/ሽ ስንት ነው? ------**
4. **የትምህርት ደረጃ? ☐ 1. ያለተማረ/ች ☐2. አንደኛ ደረጃ ያጠናቀቀ/ች ☐3. ሁለተኛ ደረጃ ያጠናቀቀ/ች ☐ 4. ከሁለተኛ ደረጃ በላይ**
5. **የትዳር ሁኔታ ምን ይመስላል? ☐1. ያገባ/ች ☐2. ያላገባ/ች ☐3. የፈታ/ች ☐4. የሞተችበት/የሞተባት**
6. **የስራ ሁኔታ ምን ይመስላል? ☐1. የመንግስት ሰራተኛ ☐2.የቀን ሰራተኛ ☐3. የግል ተቀጣሪ ☐4. ገበሬ ☐5. ተማሪ ☐6. ስራ የለውም/የላትም ☐7. ሌላ _____**
7. **ወርሓዊ የገቢ ሁኔታ (በብር)?_____**
8. **ከቤትህ/ሽ ወደ ሆስፒታል ስንት ኪ..ሜ ነው፡ ☐ 1= ≤10ኪ..ሜ ☐ 2= >10ኪ..ሜ**

ክፍል ሁለት፡ ከኤች.አይ.ቪ.. መድሐኒት ጋር የተያያዙ መረጃዎች

9. **በቀን ስንት ክኒን ነው የምትወስደው? ☐1= አንድ ☐2= ሁለት ☐3= ሰወስት ☐4= አራት ☐5= ሌላ ካለ**
10. **አሁን የሚወስዱት መጀመርያ ደረጃ መድሓኒት? ☐ 1a**=d4t/3TC/NVP; ☐ **1b**=d4t/3TC/EFV; ☐ **1c**=AZT/3TC/NVP; ☐ **1d**=AZT/3TC/EFV; ☐**1e**=TDF/3TC/EFV; ☐ **1f**=TDF/3TC/NVP
11. **አሁን ያለው የአለም አቀፍ የጤና ድርጅት የኤች.አይ.ቪ.. ኤድስ ክሊኒካል ደረጃ? ☐1. ደረጃ አንድ ☐2. ደረጃ ሁለት ☐3. ደረጃ ሦስት ☐4. ደረጃ አራት**
12. **ከሐኪምዎ ምክክር ሲያደርጉ ነፃነት ይሰመዎታል፡ ☐1. አዎ ☐2. የለም**

ክፍል ሰወሥት፡ ከኤች.አይ.ቪ.. ዕውቀትና የግል ባህርይ ተያያዥነት

13. በባለፈው አንድ ወር ውስጥ አልኮል ተጠቅሚል፡ ☐1. አዎ ☐2. የለም

14. እንደ አማራጭ መድሐኒት ፀበል ተጠቅሞ ያወቃሉ፡ ☐1. አዎ ☐2. የለም

15. ኤች.አይ.ቪ.. መዳን የሚችል ይመስለሞታል፡☐1. አዎ ☐2. የለም

16. ሁለቱ ሰዎች ኤች.አይ.ቪ.. ያላቸው ከሆነ ኮንደም መጠቀም ተገቢ ነው ብሎ ያምናሉ፡ ☐1. አዎ ☐2. የለም

ክፍል አራት፡ ከካርድ ክፍል የሚሰበሰብ መረጃ

17. የኤች.አይ.ቪ. መድሓኒት የጀመሩበት ወርና ዓ/ም...../.....

18. መድሓኒት ሲጀምሩ የመስራት ዓቅምዎ ምን ይመስል ነበር? ☐1. ጤናየን ጥሩ ነበር ☐2. ስራ መስራት የማይችል ☐3. አልጋ ላይ ተኝቶ

19. መድሓኒት ሲጀምሩ የአለም አቀፍ የጤና ድርጅት የኤች.አይ.ቪ.. ኤድስ ክሊኒካል ደረጃ? ☐1. ደረጃ አንድ ☐2. ደረጃ ሁለት ☐3. ደረጃ ሦስት ☐4. ደረጃ አራት

20. የመድሓኒት አወሳሰድና ክትትል ደረጃ? ☐1. ጥሩ ☐2. መካከለኛ ☐3. መጥፎ ደረጃ

21. መድሓኒት ሲጀምሩ ሲወስዱት የነበሩ የመድሓኒቱ ዓይነት ? ☐ **1a**=d4t/3TC/NVP; ☐ **1b**=d4t/3TC/EFV; ☐ **1c**=AZT/3TC/NVP; ☐ **1d**=AZT/3TC/EFV; ☐**1e**=TDF/3TC/EFV; ☐ **1f**=TDF/3TC/NVP

22. የሳንባ ነቀርሳ በሽታ ተይዞ ያውቃሉ? ☐1. አለው/ላት ☐2. የለውም/የላትም

23. መድሓኒት ከጀመሩት ዓይነት ቀይረዋል ☐1. አዎ ☐2. የለም

24. የቀየሩበት ምክንያት ☐1. በቲቢ ☐2. በእርግዝና ☐3. አለመስማማት/ማቃጠል

25. ሲዲ ፎር ውጤት መድሓኒት ሲጀምሩ_____ሴልስ/ሚሊ ሜትር

26. ሲዲ ፎር ውጤት መድሓኒት ከጀመሩ የሲዲ ፎር ክፍተኛ ውጤት _____ሴልስ/ሚሊ ሜትር

ክፍል ሦስት፡ <u>**የላቦራቶሪ ውጤት የተመለከቱ መረጃዎች**</u>

27. ሲዲ ፎር _____ሴልስ/ሚሊ ሜትር ኩብ

28. ቫይራል ሎድ ___ አር.ኤን.ኤ. ኮፒ/ሚሊ ሜትር ኩብ

አመሰግናለሁ!!!