PREVALENCE OF SECOND-LINE ANTIRETROVIRAL TREATMENT REGIMEN FAILURE AND ASSOCIATED FACTORS , AMONG ADULT PEOPLES LIVING WITH HIV AT ADAMA HOSPITAL MEDICAL COLLEGE, ART CLINIC, ADAMA, CENTRAL ETHIOPIA.

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A THESIS TO BE SUBMITTED TO THE DEPARTMENT OF INTERNAL MEDICINE, JIMMA UNIVERSITY FOR PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SPECIALTY CERTIFICATE IN INTERNAL MEDICINE.

DECEMBER, 2021

JIMMA, ETHIOPIA

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ABSTRACT

According to UNAIDS report of 2019, estimated 25 million people were access to antiretroviral treatment (ART). In Ethiopia more than 400,000 are taking ART. Of those patients taking ART 1.5% is on second line ART regimen. Issue of antiretroviral treatment failure becomes a major public health concern, particularly, for those on secondline. Limited studies available on magnitude and predictors of second-line treatment failure in Ethiopia.

Objective: To determine the prevalence and associated factors with second line ART regimen failure among adults living with HIV; on follow up at Adama hospital medical college in 2021 G.C.

Methods: A hospital based cross sectional study was conducted on 277 participants, by review charts, registers and interview adult patients on second line ART regimen. A pretested semi-structured questionnaire was administered by data collectors. Collected data was checked for completeness, coded and entered into Epi info Version 7 & transformed to SPSS version 25. Descriptive statistics, for characteristics of the patients. Binary logistic regression analysis was carried out for independent variables with an outcome variable to select candidate variables for multivariable analysis. Statistical association between dependent and independent variables were considered statistically significant for P-value ≤ 0.05.

Result: The prevalence of second line antiretroviral treatment failure was 5.8% (3.21-8.72). The odds of developing secondline treatment failure among those patients whose regimen were changed were about 2.6(AOR=2.56; 95%CI: 1.21-8.28) time more likely than their counter parts. Moreover the odds of developing treatment failure were more than 2 times more likely for TDF-3TC-LPV/r regimen than TDF-3TC-ATV/r,(AOR=2.41;95%CI: 1.07-6.91).Mental health problem (AOR=5.62; 95%CI: 2.52-11.86), Current CD4 count of less than 100 (AOR=3.32;95%CI: 1.63-7.91) and last BMI of less than 18.5kg/m2 (AOR=6.81;95%CI: 3.17-14.51)

Conclusions & Recommendations: The prevalence of second-line antiretroviral treatment failure was low. Low CD4, low BMI, presence of co-morbidities and mental health problem, regimen change and LPV/r containing second-line regimen were found to be associated with second-line antiretroviral treatment failure. Therefore attention should be given for strengthening integrated chronic care service delivery practice improvement to minimize second- line treatment failure.

Keywords: , Jimma University, Second line ART regimen failure, AHMC, prevalence, risk factors.

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENT

First of all, I would like to say thank you Jimma University, department of internal medicine for giving me an opportunity and support to conduct this research.

Next, I would like to say thank you to my advisors, Dr. Daniel Yilma, Dr. Gadisa Desu and Mr. Hailu Merga for their advisees, support, mentoring and encouragement they gave me, during this study from the time of proposal development to the final thesis write up.

Also I would like to thank you, my dear data collectors, and supervisors and study participants for their valuable input for this study.

Last but not least my thanks extend to AHMC administrative personnel and staffs for their being very supportive during data collection, my friends and family members who dedicated to be with me at the time I am in need of them.

TABLE OF CONTENTS

CONTENTS **PAGES**

LIST OF ABBREVIATIONS

3TC- Lamivudine

AIDS-Acquired Immunodeficiency syndrome

ABC- Abacavir

AHMC-Adama hospital medical college

ARVS-Antiretrovirals

ART- Antiretroviral Therapy

AZT-Zidovudine

CD4- Cluster of differentiation type 4

DRV-Darunavir

EFV- Efavirenz

EDHS -Ethiopian demographic health survey

FDC-Fixed dose Combination

HIV-Human Immunodeficiency Virus

IRIS- Immune Reconstitution inflammatory syndrome

JUMC- Jimma university medical center

LFU- Lost to follow up

LPV/r- Lopinavir/ritonavir

NRTI-Nucleoside reverse transcriptase inhibitors

NVP- Nevirapine

OIs-Opportunistic infections

PI- Protease inhibitors

SSA- Sub-Saharan Africa

TB-Tuberculosis

TDF-Tenofovir

UNAIDS- Joint United Nations Programme on HIV/AIDS

WHO-World Health Organization

CHAPTER ONE

1. INTRODUCTION

1.1Back ground information

The human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is a global problem, changed from life threatening to chronic disease due to the use of and availability of antiretroviral treatment (ART) .(1,26) Approximately 38.0 million people globally were living with HIV in 2019. (1) Out of 38 million 36.2 million were adults. Sub-Saharan Africa countries were account the highest burden with More than two third of the global total. (1,15) In Ethiopia the HIV prevalence in 15-49 years of age was found to be 0.9% according to 2016 EDHS. Since 1995, antiretroviral therapy (ART) has saved the lives of millions globally and has significantly decreased morbidity and mortality in peoples living with HIV/AIDS (16). Since ART first become available for free in Ethiopia in 2005, until 2013, death due to HIV/AIDS has reduced by 63%. Depending on 2019 report released from the united nation program on HIV/AIDS (UNAIDS, globally as many as 25 million people were accessing ART (1). In 2016, the federal ministry of health of Ethiopia (FMOH) reported that 1200 health facilities were providing ART, and greater than 400,000 people were using ART. From these ART users, 1.5% was on second line treatment. Most patients began on standard first-line regimen. The first-line treatment regimen consists of a combination of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) with one non-nucleoside reverse transcriptase inhibitors (NNRTI). when first line treatment failure happen, a second line treatment is implemented, utilizing two NRTIs not previously used in first-line treatment and additional protease inhibitor (PI). (16,26)

Second-line antiretroviral regimen treatment failure has very narrow options for further switching, and this is a serious concern in resource-limited settings [15]. The World Health Organization (WHO) recommends few second-line regimens as preferred ART (i.e., ritonavir-boosted atazanavir- or lopinavir-based ART and dolutegravir-based ART) [26]. Despite the limited second-line antiretroviral treatment options, many countries in SSA have financial constraints to adopt third-line regimens [15]. As a result, optimization of second-line therapies use once first line treatment failed is alarmingly essential for SSA, the epicenter of HIV/AIDS. However, many countries in SSA have no national strategic guidelines for the optimal use of second-line therapy despite rise in the secondline antiretroviral treatment failure. (15,37)

1.2 Statement of the problem

Globally, it is estimated that over 38 million peoples are living with HIV. HIV has been global challenge. (1) . Sub-Saharan Africa carries the highest burden with an estimated more than two-third of the global total. (15)(1). In Ethiopia the HIV prevalence among adults age 15-49 years was 0.9% according to EDHS 2016. Since 1995, antiretroviral therapy (ART) has saved the lives of millions globally and has significantly reduced morbidity and mortality in peoples living with HIV/AIDS. (16)

According to mathematical modeling study, 8·7-25·6 million people are expected to receive ART in 2020, of whom 0·5-3·0 million will be taking second-line ART. The proportion of patients receiving second-line therapy was highest (15·6%). In 2030, the estimated range of patients receiving ART will remain constant, but the number of patients receiving second-line ART will increase to 0·8-4·6 million (6·6-19·6%). The need for second-line antiretroviral therapy was 2 to 3 times higher if routine viral load monitoring was implemented throughout the region, compared with no further viral load monitoring scale-up.

In the past decade, rapid scale-up of antiretroviral therapy (ART) in sub-Saharan Africa (SSA) markedly decreased HIV/AIDS-related morbidity and mortality [1, 15]. Antiretroviral therapy has also prolonged the average life expectancy of HIV-infected individuals [22]. However, these importance are being challenged by the rising of HIV treatment failure rates with first or second-line antiretroviral therapies [15].

The Study done in sub-Saharan countries shows that the treatment failure rate is as high as15%. The national program data from EPHI shows that 40 out of 198 patients on second line (20%) had suspected treatment failure. (26) According to Multicenered retrospective study conducted in the Amhara region in 2017, over all incidence of second line treatment failure was 9.86 per 100 person –years. Although few studies have been done in the northern parts of Ethiopia in Amhara region but, there is no study done in other regions of Ethiopia, especially the central and southern regions of the countries in general and in the study area in particular. The second-line antiretroviral regimens treatment failure has very narrow options for further switching, and this is a serious concern in resource-limited settings [19]. As a result, the optimal use of second-line therapies after the occurrence of first-line HIV treatment failure is alarmingly essential for SSA, the epicenter of HIV/AIDS. Despite this, many countries in SSA have no national strategic

guidelines for the optimal use of second-line therapy despite the occurrence of a number of treatment failures related to the therapies [15].

Therefore identifying secondline treatment failure predictors comprehensively will help ART clinicians and other health care workers to focus on addressing those factors for patient on secondline, which assist in preventing premature switch to third line regimen which is both expensive, with higher profile of adverse effects. Over all, more studies will be needed in order to have a representative data as country, for policy makers, to have consolidated input for the public at a large.

Therefore, the objective of this study will be to determine the magnitude secondline antiretroviral treatment failure and predictors of treatment failure among adult patients on secondline at Adama hospital medical college

2.2 SIGNIFICANCE OF THE STUDY

In the context of limited options of ART drugs for treatment of secondline treatment failure, identifying the Magnitude and predictors for the development of treatment failure in patients taking second-line ART regimen, will help health workers involved in the management of peoples living with HIV; to act proactively in those potentially at risk of treatment failure and hence saves the life of thousands of patient on second-line ART and also reduce the number of patients on third- line or salvage regimen and reduce the cost of care.

Results of this study will help policy makers to further plan on prevention of secondline treatment failure and to purchase and avail third line ART regimen for those failed secondline.

The result of the study may also serve as baseline for further studies.

CHAPTER TWO

2. Literature Review

It is estimated 38.0 million people globally were living with HIV in 2019. From this ,36.2 million were adults. Sub-Saharan Africa account for More than two third of the global total burden. (1) In Ethiopia the overall HIV prevalence in 15-49 years of age was found to be 0.9% according to 2016 EDHS. Since 1995, antiretroviral therapy (ART) has saved the lives of millions globally and has markedly reduced morbidity and mortality in peoples living with HIV/AIDS(1,26). Since ART first become available for free in Ethiopia in 2005, until 2013, death due to HIV/AIDS has declined by 63%. (26)

According to 2019 report released from the united nation program on HIV/AIDS (UNAIDS, worldwide as many as 25 million people were accessing ART (1). For the year 2016, the federal ministry of health of Ethiopia (FMOH) reported that 1200 health facilities were providing ART, and more than 400,000 people were accessing ART in Ethiopia. Of these ART users, 1.5% were on second line treatment (16,26,33)

Study was done on Second-Line HIV Therapy Outcomes and Determinants of Mortality at the Largest HIV Referral Center in Southern Vietnam. All patients aged 15 years who initiated second-line ART after documented failure of first-line therapy at the Hospital for Tropical Diseases in Ho Chi Minh City were included. The primary outcome was ,death, or to a new or reoccurrence of a WHO-defined immunological or clinical failure event, whichever occurred first. Risks of treatment failure and death were evaluated using Cox proportional hazards modeling. Data from 326 of 373 patients initiating second-line ART between November 2006 and August 2011 were included, During a median follow-up of 29 months, 18.4%patients experienced treatment failure13.5% deaths. The Kaplan–Meier estimates of treatment failure after 1, 2, 3, and 4 years were 13.1%, 18.6%, and 22.8% , respectively. Older age, history of injection drug use, lower CD4 count, medication adherence were the predictors(17).

Another study which was done in 2009 in North America, assessed trends in multi-drug treatment failure and subsequent mortality among antiretroviral treatment experienced individuals. The cumulative mortality after onset of second-line virologic failure was 26% at 5

years and then decreased over time. AIDS, lower CD4+ T cell count and higher plasma HIV RNA levels were each independently associated with increased mortality. (31)

An observational cohort of patients with first-line antiretroviral therapy (ART) failure was done in a university hospital in Thailand, between January2002and December2008 Patients with first-line treatment failure . Boosted protease inhibitor and 2 nucleoside reverse transcriptase inhibitors (NRTIs), indicated by genotype results, was commonly used as second-line regimen and at 6, 12, 24, and 36 months of second-line ART, 67%, 62%, 84%, and 90% of patients achieved HIV-1 RNA <50 copies/ml.. Good adherence, high baseline CD4, and patients with early CDC staging were associated with virologic success ($P < 0.05$). Second-line antiretroviral therapy based, on genotype testing yields the good virologic and immunologic outcomes in a resource-limited setting.(32)

Study was done on Predictors of Failure on Second-line Antiretroviral Therapy with Protease Inhibitor Mutations in Uganda, from January 2008 to May 2018. Males, type of second-line ART, and Tuberculosis treatment while on second-line ART were highly predicted failure on second-line ART with PI mutations. HIV/AIDS response programs should give attention to this group of people if we are to minimize the need for expensive third-line ART. Finally more extensive explorative studies to ascertain underlying factors are needed(35,36).

Another study conducted on Protease Inhibitor Resistance on 2nd-line HIV Treatment Failure in Sub-Saharan Africa**.** From 227 included participants, 25% (N=54/216) experienced virological failure at some point during follow-up at a rate of 139 failures per 1,000 person-years. In multivariable analysis the risk factors for virological failure were: failing a non-standard non-nucleoside reverse transcriptase inhibitor (NNRTI)-based first-line regimen(37).

Systematic review and meta-analysis were also conducted to evaluate the safety and effectiveness of Atazanavir/ritonavir over lopinavir/ritonavir in HIV-1. Viral suppression below 50 copies/ml at the longest follow-up period was the primary outcome measure. Grade 2-4 treatment-related adverse drug events, lipid profile changes and grade 3-4 bilirubin elevations were used as secondary outcome measures. Atazanavir/ritonavir has 13% lower overall risk of failure to suppress the virus level < 50 copies/ml than lopinavir/ritonavir in fixed effect model. The overall risk of hyperbilirubinemia is very high for

atazanavir/ritonavir group. Atazanavir/ritonavir has a better viral suppression at lower risk of lipid abnormality than lopinavir/ritonavir (25,27).

A mathematical modeling study was done to assess, the need for second-line antiretroviral therapy in adults in sub-Saharan Africa up to 2030: Depending on this study, 8·7-25·6 million people are expected to receive ART in 2020, of whom 0·5-3·0 million will be receiving second-line ART. The proportion of patients receiving second-line therapy was highest (15·6%). In 2030, the estimated range of patients receiving ART will remain constant, but the number of patients receiving second-line ART will increase to 0·8-4·6 million (6·6-19·6%). The need for second-line antiretroviral therapy was 2 to 3 times higher if routine viral load monitoring was implemented throughout the region, compared with no further viral load monitoring scale-up.

An institution-based multicenter retrospective follow up study was conducted at three tertiary hospitals in northwest Ethiopia from March to May 2015. 356 individuals on secondline ART for at least six months were included. . The incidence rate of treatment failure was 61.7/1000 person- years. Probability of failure at the end of 12 and 24 months were 5.6 and 13.6 respectively. Out of total failure, 62.7% occurred in the first 2 years. The significant predictors of failure were , WHO clinical stage IV, CD4 cell count at switch<100, and change in weight(16)

An institution-based unmatched case–control study was conducted from February 1, 2020 to April 30, 2020 on a total of 377 clients in six public hospitals of Wollo, Amhara regional state, northeast Ethiopia. Clients whose viral load result >1,000 copies/mL in two consecutive results at least 3 months apart were cases, while ≤1,000 copies/ mL were controls. Virologic failure was predicted by poor adherence , not disclosing their HIV status, OI , CD4 count <100 cells/mm3 and 100–350 cells/mm3 low BMI <16 kg/m2 and young age 15–29 years(33) .

The studies done in Ahmara region, Northern part of Ethiopia, showed that the prevalence of second line ART failure was high and it is a major public health concern. Most of the failure occurred during the first two years of Second line ART treatment. The common predictors of secondline treatment failure, identified in most of the studies, were , advanced WHO staging, low CD4, Low BMI, poor adherence, TB, co-infection, Not given INH preventive therapy,OIS not disclosed,, LPV based Second line ART regimen, longer duration on second line and younger age(15,16,33) .

2.1 Conceptual Frame Work

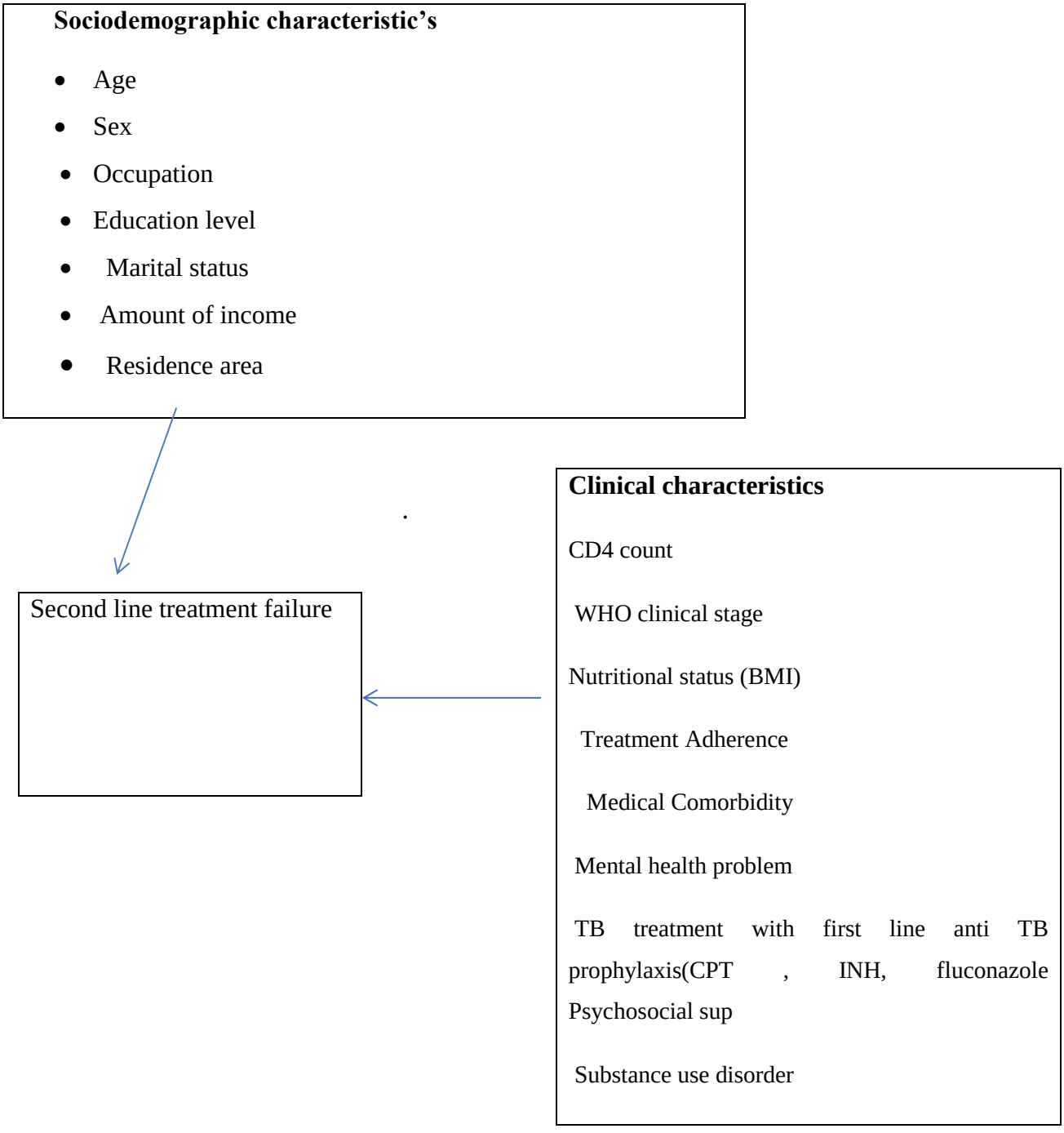

Figure 1: Conceptual framework showing the association between different variables

3.OBJECTIVES

3.1 General objectives;

- To determine the prevalence and associated factors of second-line ART failure among adults living with HIV at Adama hospital medical college in 2021.

3.2 Specific objectives

- To determine the prevalence of second-line ART failure among adults living with HIV at Adama hospital medical college during September to November 2021.
- To find out the associated factors for the development of second-line treatment failure among adults living with HIV, at Adama hospital medical college during September to November 2021

CHAPTER FOUR

4. METHOD AND MATERIAL

4.1 Study area and period

This study was conducted at Adama hospital medical college which located in Oromia region, Adama city 99 km from the capital Addis Ababa to the southeast direction, central Ethiopia in the month of October to November 2021G.C. Adama hospital medical college is one of the referral and teaching hospital in the country serving communities in Adama city and its surroundings, number of zones located to the east and south of Addis Ababa. The hospital was one of the hospital among those who started ART service earlier in the country. Recently there are more than 7500 HIV positive individuals, taking antiretroviral therapy at ART clinic in Adama hospital medical college and out of this more than 700 are on secondline. Based on figure published by the central statistical agency in 2005, Adama woreda has an estimated total population of 422,490 of whom 210,168 are men and 212, 322 are women, 64.82% of its population are urban dwellers. With an estimated area of 1,007.66 square kilometers, population density of 419.3 people per square kilometer.

4.2 Study Design

Cross-sectional study design was used.

4.3 Source population

The source population for this study was all adult patients living with HIV on HAART and on follow up at ART clinic, Adama hospital medical college.

4.4 Study Population

The study population was adult patients , on second-line ART regimen, and having follow up at ART clinic of Adama hospital medical college, seen during the study period for whom both exclusion and inclusion criteria will be fulfilled and patients are included until the required sample size is obtained.

Inclusion Criteria;

- Age >18 years
- Patients on second-line for more than six months,
- Both males and females.
- Patients who are on regular follow up.

Exclusion Criteria;

- Age < 18 years
- Duration on second-line ART < 6 months
- patients not willing to be included in the study
- Patients lost to follow up, defaulters, died or transferred out to other health facilities.
- patients with incomplete charts and records.

4.5 Sampling

4.5.1 Sample size

Sample size was calculated using the formula

$$n=\frac{Z^2 1-\alpha/2\ P\ (1-P)}{d^2}$$

$$n=\frac{(1.96)^2(0.5)(0.5)}{(0.05)^2}=384$$

Where, n = sample size

Z= confidence level(1.96) p= estimated prevalence (0.5)

d= Margin of error to be tolerated (0.05).

Since the total population is <10,000 the finite population correction formula used to determine the final sample size.

Nf= n/(1+(n/N))

n = sample size, Nf = actual sample size

N = total number of adult on secondline ART at AHMC ART clinic, (N= 741).

Therefore, the sample size will be: Nf = 384/(1+(384/741)) = 252

By adding 10% non-response rate a total of 277 patients were sampled.

4.5.2 Sampling technique

Consecutive sampling technique was used and every consecutive patient who fulfill inclusion criteria were included until the calculated sample size obtained

4.6 Variables:

4.6.1 Dependent Variables,

- Second-line ART regimen failure

4.6.2 Independent variables,

- Age
- Sex
- Occupation
- Education level
- Marital status
- Amount of income
- Residence area
- Disclosure status
- CD4 count
- WHO clinical stage
- Nutritional status (BMI)
- Treatment Adherence
- Medical Comorbidity
- Mental health problem
- TB treatment with first line anti TB during second line ART
- Provision of opportunistic infection prophylaxis(CPT , INH, fluconazole)

- Psychosocial support
- Substance use disorder
- Any prescribed or over the counter drugs taken by patient
- Duration of Second- line treatment
- Protease inhibitors and NRTI used in constructing second line regimen
- ART regimen used in firstline treatment course
- Any history of documented drug toxicity during secondline treatment course.
- Frequency of visit during follow up

4.7 Data collection tool and procedure

Semi-structured questioners were prepared in English language ,adapted from Ethiopian federal ministry of health ART intake form, patient follow up form and different registers currently in use at ART clinic. Data was collected by translating the question to the local language that the patient can understand. Three trained experienced ART provider nurses from Adama hospital medical college, ART clinic, were trained to collect data by interviewing, reviewing medical records of the patients on second- line ART regimen, different registers and necessary information on data base with prepared s structured questioners.

All relevant information such as socio-demographic characteristics, clinical information, treatment regimens, clinical and lab monitoring and outcome were recorded.

4.7 Data Analysis

The collected data were coded and entered into EPI-Info version seven and then exported to SPSS for cleaning, re-coding, transforming and analysis. Descriptive analysis was used to explore the characteristics of the participants. Data was approximately normally distributed as per the histogram and curve.

The crude associations between outcome and independent variables were assessed using binary logistic regression analysis. At this level the candidate variables for multivariate analysis were selected at P-value < 0.25. Multivariate logistic regression was applied to estimate the adjusted effects of independent variables on outcome variable. The strength of association was estimated using odds ratio along with its 95% confidence interval. Then the significance of associations

was declared at p-value < 0.05. The regression model was developed using standard model building strategy in which the effects of all predictors can be assessed simultaneously.

4.9 Data quality control

Training for data collectors before starting data collection about objective of the study, on contents of the tools and how to collect data was delivered and pre-testing of data collection instrument on few patients Adama health center ART clinic was performed. Then Data collection was undertaken by trained data collectors and Supervision of the data collection process conducted by supervisor and principal investigator by checking filled questionaries' for completeness, data keeping and management on daily basis.

4.10 Ethical consideration

Ethical clearance was obtained from Jimma University, Institute of Health Ethical Review Board. An official letter obtained from department of internal medicine and submitted to Adama hospital medical college chief clinical director office for permission. As the Information obtained was kept confidential, the patient was assured and Informed consent taken from every patient.

4.12 Dissemination plan

After Study completion and finalizing report, it will be submitted to department of internal medicine, JUMC, the ministry of health and stakeholders for possible application and publication of the research

4.13 Operational Definition

ART- is the use of one of the several classes of drugs that acts on HIV virus.

HAART-is the use of combination of three or more ART drugs to treat HIV infection.

First-line ART regimen-Is the use of three or more ART drugs given for treatment naïve patients or patients who do not have previous exposure to ART drugs.

Second-line ART regimen- is the use of three or more ART drugs given for treatment experienced patients or patients who have previous exposure to ART drugs and failed first line regimen.

CD4 T-helper calls- are integral component of body immune system, involved in helper function using immune response to invading organisms or foreign body.

WHO Clinical Stage- a staging system developed by WHO by using various clinically diagnosed disease states that have prognostic significance.

Viral Load- Used to Describe the amount of virus in a given volume of blood, usually in the viral copies per milliliter of blood.

Adherence to treatment- the degree to which the patient complies to the recommended dose, frequency and duration of treatment.

Adherence Assessment- Assessed by patient's self-report about missed doses within a month, missing more than three doses from BID doses and missing more than one dose from daily doses was considered as poor adherence

Opportunistic infections- are infection which are not common in immunologically competent individuals but occur with increasing frequency in immunocompromised individuals by taking the advantage of the weakened immune function.

ART Treatment Failure- includes; Clinical, immunological and virologic criteria's.

Secondline virologic failure- Diagnosed when a patient on second line antiretroviral regimen for more than six months, found to have two subsequent viral load >1000 copies/ml, which done three months apart with enhanced adherence support in between.

Firstline virologic failure- Diagnosed when a patient on first- line antiretroviral regimen for more than six months, found to have two subsequent viral load >1000 copies/ml, which done three months apart with enhanced adherence support in between.

CHAPTER FIVE

5. RESULT

5.1 Socio-demographic characteristics of participants:

A total of 277 participants were included in the study and 197(71.1%) were middle age, between 30-50 years and 60(21.7%) were young age 18-29 years. More than half 150(54.2%) were female and 154 (55.6%) were married. A total of 103 (37.2%) had attended secondary education while 42(15.2%) were not educated. Daily laborer accounts for 78(28 %) of the occupational status and orthodox were 182(65.7%). More than three fourth were from urban residency 229(82.7%) and 141(50.9%) had an estimated annual income <12,500 birr (**Table-1**).

Table 1: Socio-demographic characteristics of participants, the prevalence and associated factors with second-line ART treatment failure development among adults living with HIV at Adama hospital medical college in 2021.

Variables	Category	Frequency	%
Age	18-29	60	21.7
	30-50	197	71.1
	>=50	20	7.2
Gender	Male	127	45.8
	Female	150	54.2
Marital status	Single	62	22.4
	Married	154	55.6
	Widowed	40	14.4
	Divorced	21	7.6
Educational level	Primary level	97	35
	Secondary level	103	37.2
	Tertiary level	35	12.6
	Not educated	42	15.2
Occupation	Daily laborer	78	28.2
	Merchant	44	15.9
	G. Employee	57	20.6
	Private Employee	36	13
	Farmer	26	9.4

	Others	36	13
Religion	Orthodox	182	65.7
	Muslim	56	20.2
	Protestant	39	14.1
Residence	Urban	229	82.7
	Rural	48	17.3
Annual income	<12,500	141	50.9
	12,500-25,000	56	20.2
	>25,000	80	28.9

5.2 Baseline clinical characteristics at Initiation of first-line Regimen

First-line ART duration before switching to second-line were 2-5 years for 108(39%) of the participants while the regimen of the drug used by 64(23.1%) was D4t-3TC-NVP. A CD4 count of <100 was documented for 109(39.4%) patients and at the start of first line regimen 144(52%) in dividuals had WHO stage-3. The baseline functional status of 182(65.7%) were working and there were no adherence problem for about 237(85.6%) patients. On the other hand for those with adherence problem, the barrier was stigma in the community for 10(25.6%) of the participants. For near to $3/4^{th}$ 74(26.7%) the regimen of use were changed due to new regimen or drug available. The viral load at 6 & 12 month were not done during the course of first-line treatment for 274(98.9%) & 276(99.6%) respectively (**Table-2**)

Table 2: Data at initiation of first line ART regimen among adults on second line antiretroviral treatment at Adama hospital medical college in 2021

Variables	Categories	Frequency	%
Duration of first line treatment	<2 yrs	44	15.9
	2-5 years	108	39
	6-10 years	77	27.8
	>10 years	48	17.3
regimen at Initiation	1a(d4t-3TC-NVP)	64	23.1
	1b(d4t-3TC-EFV)	11	4
	1c(AZT-3TC-NVP)	61	22
	1d(AZT-3TC-EFV)	34	12.3
	1e(TDF-3TC-EFV)	63	22.7
	Others	44	15.9
CD4 at initiation	<100	109	39.4
	100-200	104	37.5
	>200	64	23.1
WHO at initiation	Stage-1	22	7.9
	Stage-2	74	26.7
	Stage-3	144	52
	Stage-4	37	13.4
Baseline functional status	Working	182	65.7

	Ambulatory	89	32.1
	Bedridden	6	2.2
Adherence problem	Yes	39	14.1
	No	237	85.6
Adherence barriers identified for those with adherence problem	Substance use	7	19.9
	Mental health	6	15.4
	Stigma	10	25.6
	Toxicity	2	5.1
	Others	14	35.9
Regimen change or substitution of drugs during firstline treatment course	Yes	84	30.3
	No	193	69.7
Reason for regimen change	New drug	74	26.7
	Toxicity	7	2.5
	New TB	3	1.1
Viral load at 6 month	<1000	1	0.4
	>1000	2	0.7
	Not done	274	98.9
Viral load at 12 month	<1000		
	>1000	1	0.4
	Not done	276	99.6

5.3 Baseline Clinical characteristics at Initiation of Second-line ART regimen

At the time of switching to the second line regimens, the CD4 count were more than 250 for near to half of the participants 133(48%) while the T-stage were stage-1 for 216(78%). The regimen was changed to second line due to virologic failure in majority 226(81.6%), but the rest 18.4% were due to immuno-clinical failure criteria. The second-line antiretroviral regimen which client initiated on was AZT-3TC-ATV/r for nearly half of cases, 131(47.3%). At this time 159(57.4%) of the patients were having high viral load of more than 10,000, while BMI were less than 18.5 for 150(54.2%) of individuals who were switched to second line regimens. Almost all 276(99.6%) were disclosed their status and more than half (56.3%) were on second-line regimen for 2-5 years (**Table-3**).

Table 3: Data at initiation of secondline ART regimen among adults on second line antiretroviral treatment at Adama hospital medical college in 2021

Variables	Categories	Frequency	%
CD4 at 2nd line	<100	34	12.3
	<250	110	39.7
	>250	133	48
T-Stage at 2nd line	Stage-1	216	78
	Stage-2	3	1.1
	Stage-3	51	18.4
	Stage-4	7	2.5
Functional status at 2nd line	Working	257	92.8
	Ambulatory	19	6.9
	Bedridden	1	0.4
Reasons for changing regimen to 2nd line	Immunologic failure	145	52.3
	Virologic Failure	**226**	81.6
	Clinical failure	88	31.8
Second line regimen initiated	2h(TDF-3TC-ATV/r)	75	27.1
	2f(AZT-3TC-ATV/r)	131	47.3
	2g(TDF-3TC-LPV/r)	11	4
	2e(AZT-3TC-LPV/r)	14	5.1

	Others	46	16.6
Viral load at Initiation of 2nd line	>10000	159	57.4
	5000-10000	22	7.9
	1000-5000	27	9.7
	Not done	69	24.9
BMI at initiation	<18.5	150	54.2
	18.5-24.9	125	45.1
	25-29.9	2	0.7
	>30		
Disclosure status	Disclosed	276	99.6
	Not disclosed	1	0.4
Mental health problem	Yes	13	4.7
	No	262	94.6
EAS before switching secondline	Yes	86	31
	No	190	68.6
Duration of 2nd line in yrs	<Two	16	5.8
	Two –five	156	56.3
	Five-ten	80	28.9
	>Ten	25	9

5.4 Prevalence of second-line ART failure and clinical characteristics of patients during second-line ART regimen.

. The second-line regimen treatment failure were developed in 16(5.8%) of the patients and for all of them enhanced adherence support were under taken before switching to third-line. During the course of the second line, 6(2.2%) of the patients were developed opportunistic infections; 17(6.1% were lost weight more than 5% and 14(5.1%) had adherence problem of which 7(50%) were due to mental health problem. Almost all were provided CPT and IPT prophylaxis 266(96%) & 275(99.3%) respectively. Similarly last WHO stage was stage-1 for 269(97.1%) while last CD4 count were more than 250 for 238(85.9%) patients. More over the last BMI were less than 18.5 in 89(32.1%) of the patients (**Table-4**).

Table 4: Data during the course of second- line ART regimen among adults on second line antiretroviral treatment at Adama hospital medical college in 2021

Variables	Categories	Frequency	%
OI	Yes	8	2.9
	No	269	97.1
Wt. loss More than 5%	Yes	17	6.1
	No	260	93.9
Adherence problem in 2nd line	Yes	14	5.1
	No	263	94.9
Adherence barriers identified during the course of secondline	Mental problem	7	2.5
	Substance use	1	0.4
	Stigma	2	0.7
	Forgetfulness	2	0.7
	Others	1	0.4
Mental problem	Bipolar disorder	1	14
	Schizophrenia	1	14
	Dementia	2	28
	Mania	3	42
	Depression(MDD)	1	14
Medical Co-morbid disease	Yes	6	2.2
	No	271	97.8

Identified co-morbid disease	HTN	3	0.4
	HF	1	0.4
	CKD	1	
	DM	1	0.4
TB Rx	Yes	2	0.7
	No	275	99.3
CPT	Yes	266	96
	No	11	4
IPT	Yes	275	99.3
	No	2	0.7
FPT	Yes	2	0.7
	No	275	99.3
Last WHO stage during the course of secondline	Stage-1	269	97.1
	Stage-2	4	1.4
	Stage-3	2	0.7
	Stage-4	2	0.7
Last CD4	<100	6	2.2
	<250	33	11.9
	>250	238	85.9
Last BMI	<18.5	20	7

	18.5-24.9	250	90
	25-29.9	9	3
Last functional status	Working	273	98.6
	Ambulatory	3	1.1
	Bedridden	1	0.4
Toxicity in 2nd line	Yes	3	1.1
	No	274	98.9
Viral load at 6 month of 2nd line	>1000	20	7.2
	<1000	254	91.7
	Not done	2	0.7
Viral load at 12 month of 2nd line	>1000	17	6.1
	<1000	258	93.1
	Not done	1	0.4
Two consecutive viral load more than 1000 copies, done 3 month apart with EAS in between	Yes	16	5.8
	No	261	94.2
Enhanced adherence support for pts. with high viral load was under taken	Yes	16	100
	No	0	0
Measurement taken	Switched to 3rd line	16	100

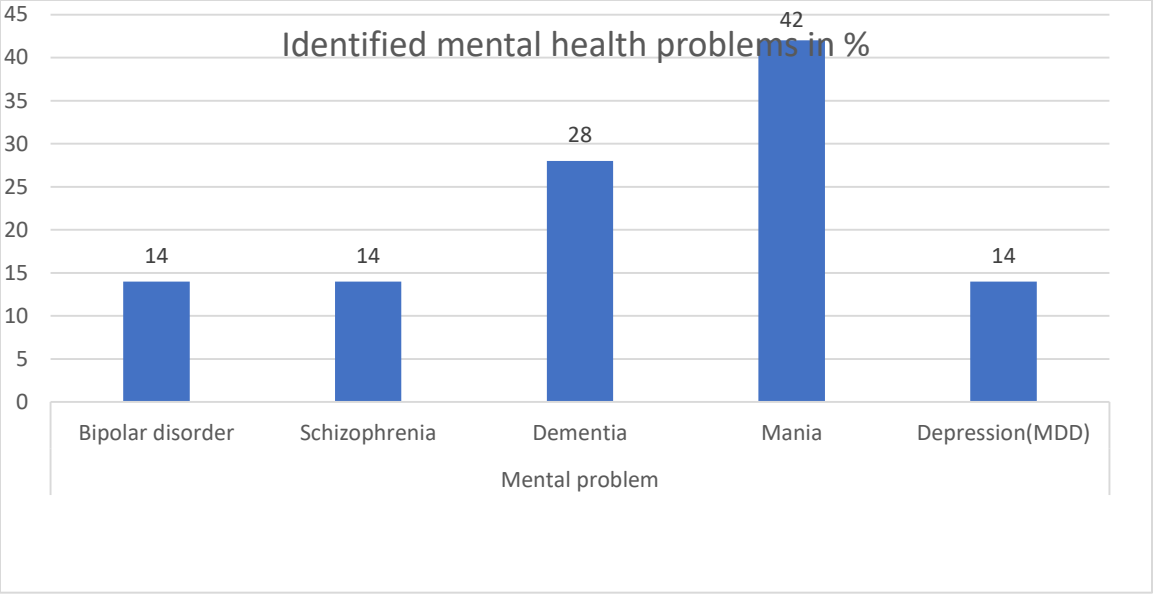

Figure 2: Identified mental health problems among patients with poor adherence to second line ART at AHMC in 2021

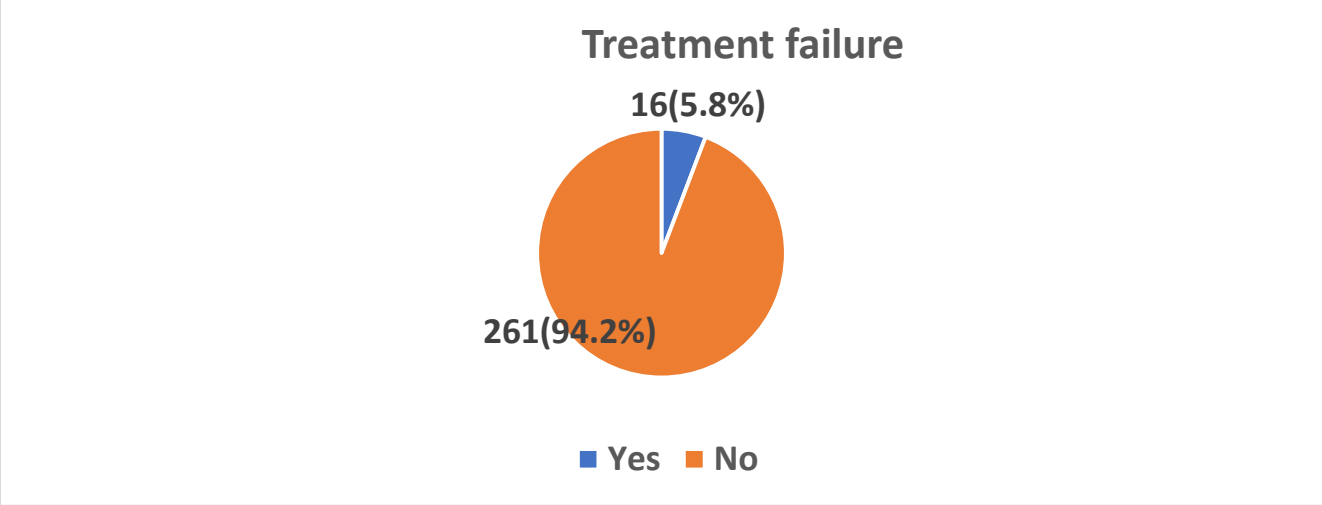

Figure 3**: Prevalence of second line treatment failure among adults on second-line antiretroviral treatment at Adama hospital medical college in 2021**

5.5 Factor Associated with second-line ART regimen failure

From those factors associated with second-line regimen failure in binary logistic regression at p-value of 0.25, regimen change during first-line treatment course, second-line regimen started, mental health problem, co-morbid disease, last CD4 and last BMI during the course of second-line were found statistically significantly associated with the second-line regimen failure. Accordingly the odds of experiencing second-line treatment failure among those patients whose regimen were changed were about 2.6(AOR=2.56; 95%CI: 1.21-8.28) time more likely than their counter parts. More over the odds of developing treatment failure were about 57% times less likely by those patients who used AZT-3TC-ATV/r regimen than those of TDF-3TC-ATV/r (AOR=0.43; 95%CI: 0.16-0.99). Additionally it was more than 2 times more likely for the user of TDF-3TC-LPV/r regimen than TDF-3TC-ATV/r (AOR=2.41;95%CI: 1.07-6.91). The odds of treatment failure were about 5 times more likely among those patients with mental health problems than those with no mental health problem (AOR=5.62; 95%CI: 2.52-11.86).

The patients who didn't develop any co-morbid disease had the odds of treatment failure of about 39% times less likely compared to their counters (AOR=0.61; 95%CI: 1.63-7.91). The individuals who had the last or current CD4 count of less than 100 were 3 times more likely to develop treatment failure than those who had the last CD4 count of more than 250(AOR=3.32;95%CI: 1.63-7.91). Those whose CD4 were less than 250 had the odds of more than 2 times (AOR=2.81;95%CI: 1.02-8.39) to develop treatment failure than those of with CD4 count more than 250. On the other hand the odds of developing treatment failure were 6.8(AOR=6.81;95%CI: 3.17-14.51) times more likely for those patients with the last BMI of less than 18.5 than those of between 18.5-24.9(**Table-5**).

Table 5:Factors associated with second- line ART regimen among adults on second-line antiretroviral treatment at Adama hospital medical college in 2021

Variables	Categories	Rx Failure		Crude and Adjusted odd ratio	
		Yes	No	COR	AOR
Regimen change	Yes	12	72	0.3(0.07-0.92)	2.59(1.21-8.28)**
	No	4	189	Ref	Ref
Second line regimen initiated	2h(TDF-3TC-ATV/r)	10	65	Ref	Ref
	2f(AZT-3TC-ATV/r)	4	127	4.88(1.63-8.17)	0.43(0.16-0.99)**
	2g(TDF-3TC-LPV/r)	2	9	0.14(0.91-0.83)	2.41(1.07-6.91)
Mental health problem	Yes	5	8	14.26(8.83-18.39)	5.62(2.52-11.86)*
	No	11	251	Ref	Ref
Co-morbid disease	Yes	1	1	Ref	Ref
	No	15	260	17(9.61-23.67)	0.61(0.09-0.93)**
Last CD4	<100	5	1	0.01(0.006-0.07)	3.32(1.63-7.91)**
	<250	7	26	18.57(10.53-21.89)	2.81(1.02-8.39)
	>250	4	234	Ref	Ref
Last BMI	<18.5	13	7	151.67(143.65-170.78)	6.81(3.17-14.51)**
	18.5-24.9	3	245	Ref	Ref

***P-value<0.001, **P-value<0.05**

CHAPTER SIX

6. 1 DISCUSSION

The main objective of this study was to determine the prevalence and associated factors of second-line ART failure among adults living with HIV at Adama hospital medical college. The prevalence of second line antiretroviral treatment failure was 5.8(3.2-8.7). This prevalence is lower than the studies conducted in Vietnam (18.4%), Uganda (23%) and North west Ethiopia was 6.17 per 100 person per year (16,17,35). This difference among these studies could be due the difference of study setting, level of clinical care, sample size and another explanation may be differences in the diagnostic criteria for treatment failure.(16,17,34&36)

Regarding associated factors with the second-line antiretroviral treatment failure in this study, type of second-line regimen used was statistically associated. The odds of developing treatment failure were less likely by those patients who used AZT-3TC-ATV/r regimen than those of TDF-3TC-ATV/r. This finding was in agreement with a study conducted in Kenya and eastern Uganda. Considering the NRTI used, this is may be due to the use of AZT during first line is associated with accumulation of Thymidine Analogue mutations (TAMs) that confer resistance to TDF and Abacavir (ABC) and increase the risk of treatment failure when TDF used as NRTI in constructing second-line regimen.. The ART guidelines have since been revised and now TDF is preferred first line NRTI because the mutations associated with it preserve future treatment options. In addition patients on AZT based regimens had better performance of physical and mental health summary score compared to those on TDF. Study also identified odds of treatment failure was more likely for the user of TDF-3TC-LPV/r regimen than TDF-3TC-ATV/r). This finding was in line with the, study done at South Africa, Eastern Uganda and North West Ethiopia. Treatment failure was significantly associated with the type of Protease inhibitor used. Patients who underwent a change to ATV boosted with ritonavir−based regimen instead of LPV/r has decreased risk to develop treatment failure. ATV is generally a well-tolerated drug with less pill burden as compared to other PIs such as LPV. The study identified also odds of experiencing second-line treatment failure among those individuals whose regimen were changed were more likely than their counter parts. This may be related to the reason for changing

regimen like; toxicity, drug- drug interaction or issue of cross-resistance may not addressed during the selection of second-line regimen.(25,26,34&36)

Moreover the study identified the odds of treatment failure were more likely among those patients with mental health problems than those with no mental health problem. This result was in line with study done in Amhara Region-Ethiopia and systematic review in Sub-Saharan Africa. .This Study also identified 14 participants, had adherence problem of which identified adherence barriers were due to mental health problem in seven of participants which account for 50% of patients with adherence problem. This can be due to the rate of second-line treatment failure for clients who had poor ART adherence was higher as compared to patients who had good ART adherence. Meanwhile patients with mental health problem May took drug for mental health problem which may be had contributed by decreasing therapeutic level of HAART and issue of drug-drug interaction should be considered. This imply that integrated mental health service for individuals on HAART and monitoring for issue of drug-drug interaction will decrease the risk of treatment failure and avoid risk of premature switch to third-line, which is a salvage therapy. The study also showed, patients with medical co-morbid disease had the increased odds of treatment failure as compared to their counterparts. This may be due to affected nutritional status, due to chronic illness or ongoing inflammation and inflammatory response, which may enable viral replication or due to drug- drug interaction or pill burden which may affect adherence to treatment. So special attention should be given for medical co-morbid and retroviral infection, in terms of treatment and follow-up.(26,33,34&36)

Another determinant associated with the second-line ART regimen failure was low CD4 count. The individuals who had low CD4 count of less than 250 were more likely to develop treatment failure than those who had CD4 count of more than 250 and the odds of failure was higher when CD4 count as low as less than 100 cell/ul. This finding in agreement with most of the studies conducted in Ethiopia, Africa, Asia and other parts of the world. This may be because a patient's immune status becomes weak, and the rate of viral replication increases compared to their immune-competent counterparts. Furthermore, clients with compromised immunity are more vulnerable to different opportunistic infections that sustain the vicious cycle of immunity and increased viral replication. This imply that, early initiation of HAART, and early detection of

treatment failure and management before patient develop advanced immune suppression may decrease further risk of treatment failure. Beside this, if patient has low CD4 count or severe immune suppression, strict adherence to infection prevention package, particularly OIs, prevention package, including providing primary and secondary prophylaxis for eligible clients. (16,23,33&34)

In addition, the study identified that those patients who had low BMI<18.5 kg/m2 were more likely to develop treatment failure as compared to those patients who had normal BMI (≥18.5 kg/m2). This result is in line with a study conducted in Amhara Regional state, Northeast Ethiopia and South Africa indicating having a low BMI was associated with treatment failure as compared to normal BMI. This is due to low BMI patients, compromising their immunity result in exposed for opportunistic and other comorbid disease so their bodies immune system could not control the viral multiplication. In other word Change in weight was the other significant predictor of failure. For a unit increase in weight in kilograms, the risk of treatment failure decreased by 8.4%. This can be explained by understanding weight gain as an indicator of good response to treatment and having a positive effect for immunity. Therefore Nutritional assessment and management integration in spectrum of chronic care and treatment of individuals on HAART will reduce risk of developing ART regimen failure.(16,23,33&36)

Cornerstone of anti-TB therapy can reduce the PI tough concentration or therapeutic level. Even though TB treatment was not identified as a significant predictor in this study, it should be noted that TB treatment may be a significant clinical contributing factor, especially if the dose of ritonavir is not adjusted to account for the reduced PI concentration associated with concomitant rifampicin.(28)

6.2 Limitation of study

The limitation of this study was recall bias of participant and the study could not show temporal relationship

CHAPTER SEVEN

CONCLUSION AND RECOMMENDATION

7.1 Conclusion – The prevalence of secondline treatment failure among adults in this study was 5.8% which slightly lower as compared to most of the studies done in sub-Saharan Africa, including North part of Ethiopia. This discrepancy might be as a result of difference of study setting, sample size, failure definition viral load cuts of point, service delivery like routine viral load monitoring and implementation of enhanced adherence support. Predictors of secondline treatment failures were low current CD4, low Current BMI, Co-morbidities, mental health problem, regimen change and type of secondline regimen initiated on.

7.2 Recommendation - Strengthening routine viral load monitoring which is already existed for the early detection of treatment failure. Strengthening EAS for those with high viral load to minimize premature switching of regimen. Improving the practice of delivery of integrated clinical services, like mental health, OIs prevention and management and nutrition assessment and management. Better to do further large scale studies

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ANNEXES

Annex 1 Consent

Topic- Prevalence of second line ART regimen treatment failure and factors associated, among adults living with HIV at Adama Hospital Medical college, ART Clinic, Adama, Central Ethiopia.

Principal Investigator: Dr. Kedir Webiti (MD)

Organization Jimma University, College of Health Sciences

Sponsor: Jimma University, institute of health sciences

Purpose of the Research project-The aim of this study is to determine the prevalence of second line ART regimen treatment failure and factors associated, among adults living with HIV, on follow up at Adama hospital medical college in 2021 G.C.

Procedure-This study involves primarily a population of patients who are on secondline and follow up at Adama hospital medical college.

Incentives/payment for participants-Will not be provided any incentives or payment take part in this project.

Confidentiality- The personal information collected from the individual patient charts will be kept confidential.

Person to contact- if you have any question you can contact:

Dr Kedir Webiti (MD, internal medicine resident) Telphone.no 0955055566. Email address kedirwebiti2008@gmail.com

Consent form (English version)

Interview code number----------

Greeting

My name is---------- I am Clinician working at Adama hospital medical college. There is one research conducting on second line ART failure and associated factors at Adama hospital medical college. Therefore, I would like to inform you that you are one of the potential participants in this study. Your participation is entirely based on your willingness and your refusal does not compromise any services you will get from this facility. If you are willing to participate in the study, we will interview you and review your charts regarding your health related general condition, Clinical and laboratory monitoring, as well as treatment services you received. I would like to assure you that, information obtained will be keep confidential, study has no any harm to you and no any payment. Do you agree to participate in this study?

If the participant agrees to participate in the study, proceed with interview after he/she has signed the consent form.

I, Mr/Ms/---/----------have been told the contents of this research and I have adequate information and understood well regarding its contents and I do agree to participate the study.

Name of the participant----------Signature---------- Date----------

If the participant says" No I do not agree to participate in the study" thank him or her and stop.

Thank you!

Name of interviewer----------Date ----------/-------/

Unkaa hirmanna qorannoof eeyyemama tahu, ittin gafataamu/Consent form/ (Afaan Oromoo version)

Lakkofsa koodii Gaafii fi deebii----------

Nagaaya gafaachuun eegalu… Dura dursee akkam nagaya jirtu!

Maqaan koo---------- Ani ogeessa fayyaa hospital kolleejjii fayyaa adaama hojatudha/ttudha/. Qorannoo tokkotu adeemsifama jira hospital kanattii. innis Waa'ee facaatii hojjachu dadhabu qorichaa farra HIV sadarkaa lammaffaa fi wantoota sanan wal qabatan irratti. Kanafuu, Ati/ isin/ namoota qorannoo kana kessatti hirmachuu dandahan kessaa tokko tahu dandeessuu. Walumagalatti hirmannan keessan, fedhii kessanin murteeffama, akkasumas hirmachuu dhabuun garuu tajajila dhabbata kana kessatti argachuu qabdan kamiyyuu isin hin dangeessuu.Yoo hirmaachudhaf fedhii qabattan/tte/, gaafii fi deebii isinif godhama, akkasumas ragaa barreefama kan yaalaa fi hordooffi fayya keessanin wal qabatu ni ilaalla . Dhumaratti wanti ani sif/isinif mirkaneessuu barbadu, ragaleen funaanamani kannin, iccitin sirriti kan eeggamu tahu isati fi qoraannoon kuni midhaa kamu kan hin qabne fi akkasumas kanfaalti kan hin qabne tahu isati.. Qoraannoo kana kessatti hirmachuuf fedhii qabdu ? A) eeyyen, B) lakkii

Yoo hirmaatan fedhii hirmachu qabate, wal gale, erga mallattoon unkaa kanarratti mallatteesse booda gaafii fi deebiin ni godhama.

Ani Obboo/Addee/---/----------waa'ee qabiyyee qooraanoo kana sirritti naaf ibsameera, akkasumas hubadheen jira . kanafuu qoraannoo kana kesssattii hirmachuuf, itti wal galu koo mallattoodhan ni mirkaneessa.

Maqaa hirmaata/ttu/----------Mallattoo---------- Guyyaa----------

Yoo hirmaatan, "itti wal hin galuu qoorannoo kana keessatti hirmachuf" jedhe, galaateefadhuti adda kuti gaafii fi deebii.

Galaatooma!

Maqaa nama gaafii fi deebii godhe:----------Guyyaa ----------/-------/-----

Annex 2-Questionnaries

Data collection Instrument on the prevalence of second line ART regimen treatment failure and factors associated, among adult individuals on HAART at Adama hospital medical college in 2021 G.C.

Instruction- Dear Data collector, the objective of this study is to determine the prevalence and associated factors for the development of secondline ART treatment failure among adults on secondline. The result of this study will help us to know the magnitude of the problem and factors associated with the treatment failure and then develop preventive strategies. So, you are kindly requested to revise charts thoroughly and interviewing the patients, then record on the following questionnaire.

Research Code number----------

Part 1- Sociodemographic Data

1.Card number----------

2.Age in years----------
3.Gender-1 Male 2 Female
4.Marital status
- Single
- Married
- Divorced
- Widowed

5.Level of Education-

- Primary education
- Secondary education
- Tertiary education
- No education

6. occupation---- specify----------

7.Religion------- specify----------

8. Residence

- Urban
- Rural

9. Average estimated annual in come

a) < 12,500 birr

b) 12,500-25,000

c) >25,000

Part 2- Data concerning first line ART

1 -Duration of first line therapy (in months) ----------
2.ART regimen at initiation of therapy----------
3. CD4 count at initiation of therapy----------
4.WHO clinical stage at the initiation of therapy:
a) stage 1
b) stage 2
c) stage 3
d) stage 4
5. Baseline functional status during started on firstline ART.
a) Working, b) Ambulatory, c) Bedridden
6. Any adherence problem during the course of first line ART regimen therapy
a) Yes
b) No
7. If yes, for adherence problem, then what was the identified barriers for adherence ? specify----------
8. Any regimen changes during firstline regimen treatment?
a) Yes
b) No

9. If yes, for regimen change, what was reason? specify----------

10. Viral load at 6 months of firstline treatment initiation :
a) < 1000 copies/ ml b) > 1000 copies/ml
11. . Viral load at 12 months of firstline treatment initiation :
a) < 1000 copies/ ml b) > 1000 copies/ml
12.Any medical comorbidity identified
a) yes b) No

Part 3- Data at the beginning of secondline ART regimen

1.Duration of firstline ART regimen (in months) ----------
2. Reason for changing to second line regimen:
a) virologic failure
b) Immunologic Failure
c) Clinical failure
3 What was CD4 cell count at initiation of secondline ART regimen?
a) < 100 cell
b) <250
c) >250

4. What was T- staging of the patient when he/she started on secondline ART

a) Stage 1 c) stage 3

b) Stage 2 d) stages 4

5.) Functional status of the patient during beginning of secondline

a) Working, b) Ambulatory c) Bedridden

6. What was the secondline ART patient initiated on? Specify----------

7. Viral load at initiation of secondline ART regimen----------

8. BMI of patients at initiation of secondline ART regimen:
a) < 18.5kg/m2 b) 18.5-25kg/m2 c) 25-30kg/m2 d) >30kg/m2

9. What was the disclosure status when patient initiated on secondline ART
a) Disclosed b) yet not disclosed

10.Did the patient assessed for the need of psychosocial support and linked
a) Yes b) No

11. Any mental health problem assessed and identified
a) Yes b) No

12. Implementation of Enhanced adherence support before switching to secondline.
a) yes b) No

Part 4- Data during the course of secondline regimen.

1-Duration of secondline ART regimen therapy (in months) ----------

2.Any opportunistic infection diagnosed during secondline ART follow up period,
a) Yes b) No

3. If yes for the above question specify. ----------

4. Any history of significant weight loss (>5% of body weight in six months) -------
a)Yes b) No

5. Any adherence problem during the course of secondline ART regimen therapy
a) Yes b) No

6 If yes for the above question; Specify the identified adherence barriers----------

7. Any history of comorbid diseases. a) Yes b) No

8. If yes for the above question : specify (e.g., DM, cardiac, mental health problem---etc.)----------

9. Any prescribed or over the counter drug taken while patient on secondline ART
a) Yes b) No

10. Any substance use disorder identified: a) Yes b) No

11. If yes for the above question, specify----------

12. History of TB-treatment with firstline anti TB drugs during the course of secondline ART a) Yes b) No

13.provision of opportunistic infection prophylaxis(CPT,IPT, FPT)
1. cotrimoxazole a) Yes b) No

2. INH a) Yes b) No

3. Fluconazole a) yes b) No

14. Frequency of follow up during the course of secondline therapy

a) Every month, b) every 2 months, 3, Every 3 months

15. Last WHO staging while patient on secondline ART

a) Stage T1 b) Stage T2 c) Stage T3 d) Stage T4

16. Last CD4 count while on second line ART

a) <100 b) <250 c) >250

17 Last BMI of the patient while on Secondline ART

a) <18.5 kg/m2 b) 18.5-25kg/m2 c) 25-30kg/m2, d) > 30kg/m2

18 What is the last functional status of the patient?

a) Working, b) Ambulatory c) Bed ridden

19. Any documented drug toxicity that affects adherence to treatment.

a) yes b) No

20. Viral load at 6th month of secondline ART initiated

a) >1000 copies/ml b) <1000 copies/ml

21. Viral load at 12th month of secondline ART treatment

a) >1000 copies/ml b) <1000 copies/ml

22. . Last Viral load value while the patient on secondline ART treatment

a) >1000 copies/ml b) <1000 copies/ml

23 Does the patient has two consecutive viral load value greater than(>) 1000 copies/ ml which done 3 months apart with enhanced adherence support in between

a) Yes b) No

24. Did Enhanced adherence support undertaken for patients with high viral load value.
a) Yes b) No

25. Measurement taken for those with evidence of treatment failure.

a) on Enhanced adherence support, b) switched to Third line, c) no action taken

Name of Data collector----------

Signature----------

Date of Data collection----------

Name and signature of supervisors----------