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Prevalence of, and Factors Influencing First Line Antiretroviral Treatment Failure among Adult HIV Patients at Antiretroviral Treatment Clinic of Mettu Karl Referral Hospital, South Western, Ethiopia: A Prospective Cross Sectional Study, 2021

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Abstract

Background: Antiretroviral treatment failure is defined as progression of disease and high risk of mortality after beginning of highly active anti-retroviral therapy. First-line ART failure has emerged as a growing concern. ART failure is a major challenge to HIV/AIDS management in resource-limited settings including Ethiopia where the diagnosis and management of ART failure is a key problem. Principal factors involving fist-line antiretroviral regimen failure include poor adherence to medication, younger age, lower baseline CD4+ count and higher baseline viral load.

Objective: To ascertain prevalence, and factors influencing first line anti-retroviral treatment failure among human immunodeficiency patients at anti-retroviral treatment clinic of Mettu Karl Referral Hospital.

Methods: An institutional based prospective cross sectional study design was conducted from April 03/2021 to June 04/2021. Data was collected through employing check list and semi-structured questioner, and then the collected data was coded and analyzed by statistical packages for social sciences 25.0 version statistical software. Both bi-variable and multivariable analysis performed to determine the association between outcome and predictors variables. In the multiple logistic regression models significant association was declared at p-value < 0.05.

Results: The magnitude of first line anti-retroviral treatment failure among human immunodeficiency patients was 29.3%.At the time of study almost half of patients, 55(41.4%) were married and 85 (63.9%) were living in urban. Age ≥ 42 years (AOR: 2.04; 95%CI:1.0761-5.902;P = 0.002), rural residents (AOR: 3.51; 95%CI:1.1.951-11.4 30; P = 0.001),

divorced (AOR:1.962; 95%CI:0.427-2.942; P = 0.008), AZT + 3TC + NVP at initial ARV regimen follow up (AOR:2.980; 95%CI: 1.1842-1.749; P = 0.006), duration of ARV treatment ≥ 6 years (AOR:3.15; 95%CI: 2.963-7.028; P = 0.006), and base line WHO clinical stages III/IV (AOR:3.97; 95% CI:1.045-14.937; P = 0.009) were predictors of first line anti-retroviral treatment failure among HIV patients at ART clinic.

Conclusion and recommendation: The magnitude of first line anti-retroviral treatment failure among HIV patients was high. The initial regimen for HIV/AIDS infected patients were D4+3TC + EFV. Age greater than forty two years, rural residents, divorced, AZT + 3TC + NVP at initial ARV regimen follow up, duration of ARV treatment ≥ 6 years and base line WHO clinical stages III/IV were the factors associated with 1st line ART failure. Health care workers should have to educate the patients on how the disease where prevented and controlled and government also implement new drafts on the drug efficiency.

Keywords

1st line ART Failure, Prevalence, Influencing Factors, ART Clinic, Mettu Karl Referral Hospital, Ethiopia

Abbreviations

ART: Anti-retroviral Therapy; ARV: Antiretroviral; TB: Tuberculosis; cART: Combination Antiretroviral Therapy; CD4: Cluster of Differentiation 4; HAART: Highly Active Antiretroviral therapy; HIV/AIDS: Human Immune Virus/Acquired Immune Deficiency Syndrome; PLWH: People Were Living with HIV Infection; SSA: Sub-Saharan Africa; UNAIDS: Joint United Nations on HIV/AIDS; WHO: World Health Organization

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Introduction

Human immunodeficiency virus is responsible for a worldwide pandemic, and it is the cause of acquired immune deficiency syndrome (AIDS). All HIV-infected adults and adolescents started ART when their CD4 count was < 500 cells/mm³ irrespective of the World Health Organization (WHO) clinical stage, WHO clinical stages 3 and 4 irrespective of CD4 cell count, active tuberculosis disease irrespective of CD4 cell count, all HIV positive pregnant and breastfeeding women irrespective of CD4 count and all HIV-infected partners of sera-discordant couple regardless of CD4 cell count (to reduce the risk of HIV transmission to the negative partner). First-line ART regimen is recommended, which is simplified and less toxic, and more convenient regimens as fixed-dose combinations are available. Preferred first Line regimens drugs are TDF + 3TC + EFV (FDC) while Alternative regimen are AZT + 3TC + EFV, AZT + 3TC + NVP and TDF + 3TC + NVP [1]. Treatment failure occurs when a combination of the ARV regimen fails to control HIV infection. This could be virologic, immunologic and/or clinical failure [2]. Antiretroviral (ARV) treatment failure is defined as progression of disease and high risk of mortality after beginning of HAART. It can be assessed by clinical failure (occurrence of new infections (OI) or malignancy, symptomatic of clinical disease progression; recurrence of previous OI, onset, or recurrence of WHO stage IV (& certain stage III) conditions, etc.), immunologic failure (a decline in the CD4 + T cell count), or virological failure (The inability to maintain suppression of viral replication to an HIV RNA level < 1000) either in combination or discordantly. Clinical and immunologic criteria have been used for assessing treatment failure in the absence of viral load (VL) test [3,4]. The patients who had failed for fist-line drug are 46% more likely to fail again for second-line drugs and are attributed to the higher number of side effects and have greater likelihood of experiencing drug resistance and treatment fatigue as a result of being on treatment longer [5]. Previous studies reported that various factors including being male gender, illiterate, widower, poor adherence and treatment interruption, WHO clinical stage III and/or IV, low CD4 cell at ART initiation, presence opportunistic infections, low BMI, taking ARV regimen before ART initiation, taking Stavudine and Zidovudine (AZT) based regimen, TB co-infection, substance use and longer duration on ART were significantly associated with first line ART failure [6]. The World Health Organization cites poor access to services, complex drug regimens, pregnancy, mental health disorders, substance abuse, and weak social support as major barriers to adherence [7]. Globally, it is estimated that 36.9 million people were living with HIV during 2017. Sub-Saharan Africa (SSA) remains significantly affected, accounting for 69.5% of the people living with HIV (PLWHA). Ethiopia is among the SSA countries most affected by HIV/AIDS with an estimated 710,000 people living with HIV in 2016 [8]. The introduction of highly active anti-retroviral therapy was a critical milestone in the history of HIV disease resulting in a dramatic reduction of morbidity and mortality, and improvement in the quality of life of PLWHA [9]. In the sub-Saharan Africa, many patients who experience virological failure do not switch to potent second line regimens due to re- source limitation, yet those who remain on a failing first-line regimen experience dis proportionately higher morbidity and mortality compared to those who switch [10]. Sub-Saharan Africa is a region highly affected by HIV epidemic. Ethiopia is one of the Sub-Saharan African countries with the highest numbers of people affected by the problem [8]. In Ethiopia, there were 710,000 patients infected with HIV/AIDS in 2016. Around 404,405 HIV patients were on an antiretroviral therapy (ART) and around 20,000 AIDS-related deaths were reported in the same year [11]. In Ethiopia, viral load determination and guiding ART treatment with the gold standard test (viral load) has started recently because of resource limitation. Consequently, there is limited data on treatment failure and its associated risk factor. The available studies [12] were conducted on first-line antiretroviral treatment failure. These studies didn't address second-line and immunovirological discordance of treatment failure Studies in East Africa have shown a high prevalence of immunologic failure ranging from 8% to 57% among clients on first-line HAART, and furthermore, the magnitude increases as the time of follow-up increases [13]. The prevalence of first-line ART failure differs significantly across countries depending on the criteria (clinical, immunological or virologic) used for its diagnosis. The viral load cut-off points to diagnose treatment failure also vary in different countries. The first-line ART virologic failure rate in Africa was 7.1 per 100 patient years of follow-up [14]. In Ethiopia, studies reported virologic failure rates ranging from 5.3 to 19% [15], and the percentage of patients switched to second-line ART was 1.5% in 2013 [16]. This study were identify the risk factors associated with first-line ART failure and increase the treatment efficacy that permit better use of these potent drugs by, avoiding unnecessary side effects of first-line drug, prevent drug resistance, and decrease economic burden, especially in a resource-limited setting like Ethiopia.

Methodology

Study design, area and subject

An institutional-based prospective cross sectional study was conducted from April 03/2021 to June 04/2021 in MKRH, Oromia Regional State; Southwestern, Ethiopia, located at 600 km from Addis Ababa. The study population of our study was all HIV-infected adult patients who were taking ART during the study period at study area. Those who had been on ART for ≥ 6 months, those who had documented CD4 cell count, those who had viral load measurement at baseline and 6 months

were included in the study. Who had pregnancy and breastfeeding history the past 6 months while on treatment, at 6 months' visit or had missing values of CD4 cell count, viral load at baseline and 6 months' visit, patients who were switched to 2nd line as a result of side effects to antiretroviral drugs in 1st line treatment were excluded.

Sample size calculation and sampling technique

The sample size was determined by using the single population proportion formula: The sample size was determined based on "P" value which was taken from Harar public hospitals, Eastern Ethiopia, P = 0.21, or 21%. $n = \frac{(za/2)2\ p(1-p)}{d2}$, n = sample size, P = prevalence of 1st line ART failure, d = margin of sampling error tolerated, z = the standard normal value at confidence interval of 95%. n = $n = \frac{(1.96)^2\ (1-0.21) \times (0.21)}{(0.05)^2} = 255$. Since the total number of first line ART failure patients medical record cards from January 2021 to March 2021 was less than 10,000, which was 229 reduction formula (correction formula) was applied as follow; n_f = n/ (1+(n/N)), n_f = 255/(1 + (255/229) = 121. When 10% contingency is added to minimize non response rate, then final sample size was found to be 133. A systematic random sampling technique was applied to select the patients 1st line ART failure by determining the sampling interval. Sampling interval was calculated by (K = N/n), then K = 229/133 = 1.7th~2th. Then, the first patients 1st line ART failure was selected by the lottery method from the 1st line ART failure patients.

Variables

The outcome variable for this study was the occurrence of 1st line ART failure, and the predictors was socio demographic factors (age, sex, educational status, monthly income, marital status, family size), and clinical characteristics (adherence, advanced WHO stage, CD4 count, regimen change, function al status, co-infection and disclosure).

Measurements

A well-structured standard checklist and questionnaire was used to collect relevant information from patient face to face and their charts. Data was extracted from all eligible patient medical charts and patients' response. The data collection tool contains patient socio-demography, the question was having five parts that are socio- demographic characteristics, clinical characteristics of patients, laboratory measures and ART treatment related conditions, health facilities related questions and behaviors of HIV/AIDS patients those who were on ART. All the data collection process was conducted by recruited nurses and monitored by the PI at the hospital. Treatment failure was defined according to World Health Organization (WHO) 2010 criteria by at

least 1 of the following in a patient taking 2 NRTIs and 1 NNRTI for 1 year or more:1) New WHO clinical stage 3 or 4 disease (with CD4 count < 200 cells/mm³ and viral load > 400 copies/ml); 2) CD4 count of < 100 cells/mm³ at 12 months of treatment OR a fall to baseline (nadir) or below baseline CD4 count OR a 50% fall from on-treatment peak value; 3) A viral load > 5000 copies/ml. The 1st line ART non-adherence was measured by patient self-report based on pills count. This adherence has three categories that is poor adherence (< 85%) if the patient miss to take less than 6 of 30 prescribed doses or > 9 doses of 60 prescribed dose, fair adherence (85-94%) if the patient miss to take 3-5 of 30 prescribed doses or 3-9 doses of 60 prescribed dose and good adherence (> 90%) if the patient miss to take ≤ 2 of 30 prescribed doses or ≤ 3 doses of 60 prescribed dose [1]. In order to assure quality of data important measures were undertaken including: the patient card number was used, to check for if there is invalid and incomplete pertinent response and these cards were also coded so over or under count was not matter. The data collected was checked for completeness and consistency on daily basis.

Data analysis

The screened data was coded and analyzed through employing statistical packages of social sciences version 25.0 statistical Software. Categorical variables were expressed by percentage and frequency. Bi-variate and multivariate logistic regression analyses were conducted to determine associated risk factors of 1st line ART failure. Variables with a p-value of < 0.25 on bi-variate analyses were selected for multivariate logistic regression analysis to identify independent risk factors of 1st line ART failure. Variables having a P-value ≤ 0.05 on the final model of multivariate logistic regression were considered as significantly associated risk factors for 1st line ART failure.

Operational Definitions

ARV treatment failure is progression of disease and high risk of mortality after beginning highly active antiretroviral therapy [1].

Clinical failure New or recurrent WHO clinical stage 4 conditions, or new or recurrent WHO stage 3 with pulmonary TB or severe bacterial infections [17].

Good adherence was defied as patients taking antiretroviral drug on time, regularly ≥ 95%, while < 95% was categorized as poor adherence [18].

Results

Socio-demographic characteristics and socio-economic condition

A total of 133 HIV/AIDS patients who received ART were enrolled in the study. Of these, 79(59.4%) of them were male and 54(40.6%) were female. One-third

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Table 1: Socio-demographic characteristics and socio-economic condition of the patients attending ART clinic at MKRH, 2021 (n = 133).

Variables	Category	Frequency	Percent
Age	15-29 years	42	31.6
	30-35 years	43	32.3
	36-41 years	30	22.6
	≥ 42 years	18	13.5
Sex	Male	79	59.4
	Female	54	40.6
Residency	Urban	85	63.9
	Rural	48	36.1
Income(ETB)	<1500	103	77.4
	≥1500	30	22.6
Marital status	Single	55	41.4
	Married	32	24.1
	Divorced	37	27.8
	Widowed	9	6.8
Educational status	Unable to read and write	61	45.9
	Grade 1-8	40	30.1
	Grade 9-12	17	12.8
	Diploma	12	9.0
	Degree, and above	3	2.3
Living condition	Alone in house	62	46.6
	Alone in street	9	6.8
	With family/friend	48	36.1
	Others	14	10.5
Magnitude of 1st line ART failure	Yes	39	29.3
	No	94	70.7

Table 2: Clinical characteristics of the patients attending ART clinic at MKRH, 2021 (n = 133).

Variables	Category	Frequency	Percent
Functional status	Working	103	77.4
	Not working	30	22.6
WHO stage of HIV	Stage I	24	18.0
	Stage II	67	50.4
	Stage III/IV	42	31.6
Body mass index	≤ 16 kg/m^2	36	27.1
	16.01-18.5 kg/m^2	72	54.1
	> 18.5 kg/m^2	25	18.8
Opportunistic infection	Yes	79	59.4
	No	54	40.6
OI after initiate ART	Yes	48	36.1
	NO	85	63.9

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TB co infection	Yes	73	54.9
	No	60	45.1
Chronic non communicable diseases during on first line ART	Yes	67	50.4
	NO	66	49.6
Presence of malnutrition during on first line ART	Yes	36	27.1
	No	97	72.9
Cotrimoxazole taken	Yes	90	67.7
	No	43	32.3

43(32.3%) of the patients were within the age group of 30-35 years. The majority of 103(77.4%) respondents were earned monthly income < 1500 ETB. At the time of study almost half 55(41.4%) of patients were married and 85(63.9%) were living in urban. Slightly less than half 63(45.9%) of participants educational status were unable to read and write, and majority 62(46.6%) of patients dwell alone in the house. The magnitude of first line anti-retroviral treatment failure among HIV patients was 29.3% (Table 1).

Clinical characteristics of the patients

Preponderance 103(77.4%) of respondents were working and half 67(50.4%) of respondents HIV/AIDS clinical WHO stage was Stage II. Majority 72(54.1%) of participants body mass index were between 16.01-18.5 range, and 79(59.4%) patients had opportunistic infection. Above half 85(63.9%) of participants hadn't OI after initiate ART. Majority 73(54.9%) of patients had TB co infection, and half 67(50.4%) patients were have chronic non communicable diseases during on first line ART. Only less than one-third 36(27.1%) of respondents had have presence of malnutrition during on first line ART, and majority 90(67.7%) patients were take cotrimoxazole (Table 2).

Treatment related factors of patients

The initial regimen for HIV/AIDS infected patients were D4T+3TC+EFV (1b) 55 (41.0%), and majority 67(60.4%) of patients were substitute the medication none. Side effects 59(44.4%) were the major reason that why the patients substitute their regimen. Half 67(50.4%) of patients adherence status were fair, and 67(50.4%) were keeping appointment schedule through came on time. Slightly less than half 73(54.9%) of respondents weren't have diagnosis of recurrent pneumonia (> 2 episodes), and 72 (54.1%) of patients diagnosed not to have antiretroviral treatment failure (Table 3).

Multi-variate logistic regression of treatment failure among 1st line ART failure

All variables showing a P-value of less than 0.25 in uni-variate analysis were further tested in the multivariate logistic regression models, on the final model of multivariate logistic regression. Prevalence of first line anti-retroviral treatment failure among HIV patients was highest among patient ≥ 42 years were (AOR: 2.04; 95%CI: 1.0761-5.902; P = 0.002) 2 times more likely develop treatment failure than other age category. ART users who dwelled in rural areas were two times more likely to develop first-line ART failure than those reside in urban (AOR: 3.51; 95% CI: 1-11.430; P = 0.001) 3.5 times more likely develop treatment failure than those in lived in urban. Regarding marital status divorced (AOR: 1.962; 95%CI: 0.427-2.942; P = 0.008) 2.9 times more likely develop treatment failure than the left marital status. HIV/AIDS infected patients who were on AZT + 3TC+NVP (1c) at initial ARV regimen follow up (AOR: 2.980; 95%CI: 1.1842-1.749; P = 0.006) 3 times more likely develop treatment failure than those who taken others regimen. Patients whose baseline WHO clinical stages III/IV (AOR: 3.97; 95%CI: 1.045-14.937; P = 0.009) were 3.9 times more likely develop treatment failure than baseline WHO clinical stage I and II and patients whose duration of ARV treatment ≥ 6 years (AOR: 3.15; 95%CI: 2.963-7.028; P = 0.006) were 3.15 times more likely develop treatment failure than those who had duration of ARV treatment < 6 years (Table 4).

Discussion

Treatment failure is one of the causes of mortality and development of drug resistant viral strains potentate a significant challenge globally [19,20]. Sustainable treatment failure is related to difficulty to delivering quality care, the emergence of drug resistant viruses which limits the treatment option and increases the threat of morbidity and mortality. The identification and management of first-line ART failure is a key challenge for HIV programs in resource-limited setting. Staying on a failing first-line therapy is associated with an increased risk of mortality [21].

The present study revealed, the magnitude of first-line ART treatment failure was 29.3%. This study was higher than the survey conducted in Harar public hospitals 21%, Asella Referral Hospital 27% [22,23]. The difference was more respondents in recent survey was due-to poor patient-health care workers, no adequate education and counseling about the disease, limited access to ART as

Table 3: Treatment related factors of patients attending ART clinic at MKRH, 2021 (n = 133).

Variables	Category	Frequency	Percent
Initial ARV regimen	D4T + 3TC + NVP (1a)	36	26.9
	D4T + 3TC + EFV (1b)	55	41.0
	AZT + 3TC + NVP (1c)	28	20.9
	AZT + 3TC + EFV (1d)	9	6.7
	Others	6	4.5
Duration of ARV treatment	< 6 years	47	35.3
	≥ 6 years	86	64.7
Number of drug substitutions made	None	67	60.4
	Once	60	45.1
	Twice or more	6	4.5
Reason for drug substitution	Side effects	59	44.4
	Risk of pregnancy	24	18.0
	Due to new Tuberculosis	14	10.5
	New drug available	6	4.5
	Drug stock out	18	13.5
	Others	12	9.0
Adherence status	Good	36	27.1
	Fair	67	50.4
	Poor	30	22.6
Keeping appointment schedule	Came on time	67	50.4
	Came late	30	22.6
	Came early	36	27.1
Diagnosis of recurrent pneumonia (> 2 episodes)	Yes	60	45.1
	No	73	54.9
Diagnosed to have antiretroviral treatment failure	Yes	61	45.9
	No	72	54.1

Table 4: Multi-variate logistic regression of treatment failure among patients attending ART clinic at MKRH, 2021 (n = 133).

Variables	Category	n (%)	COR (95%CI)	AOR (95% C.I)	p-value
Age	15-29 years	42 (31.6)	Ref	Ref	
	30-35 years	43 (32.3)	0.243 (0.195-2.830)	0.675 (1.823-1.724)	0.179
	36-41 years	30 (22.6)	0.947 (0.690-3.864)	1.021 (0.047-1.439)	0.674
	≥ 42 years	18 (13.5)	1.053 (0.867-9.142)	2.04 (1.0761-5.902)	0.002
Sex	Male	79 (59.4)	Ref	Ref	
	Female	54 (40.6)	0.461 (0.289-2.157)	0.926 (1.0281-1.034)	0.496
Residency	Urban	85 (63.9)		Ref	
	Rural	48 (36.1)	2.819 (1.708-12.432)	3.51 (1.951-11.430)	0.001
Marital status	Single	55 (41.4)	Ref	Ref	
	Married	32 (24.1)	0.971 (0.537-2.013)	1.53 (0.183-1,8740)	0.951
	Divorced	37 (27.8)	1.016 (0.920-8.690)	1.962 (0.427-2.942)	0.008
	Widowed	9 (6.8)	0.614 (0.152-4.916)	0.385 (0.089-1.259)	0.509
Living condition	Alone in the house	62 (46.6)	Ref	Ref	
	Alone on the street	9 (6.8)	0.418 (0.317-3.197)	0.75 (0.042-1.017)	0.0543
	With family/friends	48 (36.1)	0.752 (0.479-2.519)	1.03 (0.073-1.079)	0.193
	Others	14 (10.5)	0.163 (0.019-3.185)	0.431 (0.741-1.658)	0.860

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Initial ARV regimen	D4T + 3TC + NVP (1a)	36 (26.9)	Ref	Ref	
	D4T + 3TC + EFV (1b)	55 (41.0)	0.815 (0.724-5.317)	1.290 (0.1942-1.843)	0.745
	AZT + 3TC + NVP (1c)	28 (20.9)	1.932 (1.420-7.308)	2.980 (1.1842-1.749)	0.006
	AZ + 3TC + EFV (1d)	9 (6.7)	0.393 (0.162-4.016)	0.968 (0.047-1.123)	0.906
	Others	6 (4.5)	0.183 (0.021-3.901)	0.371 (0.153-1.007)	0.213
Duration of ARV treatment	< 6 years	47 (35.3)	Ref	Ref	
	≥ 6 years	86 (64.7)	2.931 (2.042-13.510)	3.15 (2.963-7.028)	0.006
Diagnosis of recurrent pneumonia	Yes	60 (45.1)	Ref	Ref	
	No	73 (54.9)	0.924 (0.631-9.012)	1.47 (0.342-1.732)	0.756
OI after initiate ART	Yes	48 (36.1)	Ref	Ref	
	No	85 (63.9)	0.714 (0.417-6.710)	0.915 (0.032-1.421)	0.820
WHO stage of HIV	Stage I	24 (18.0)	Ref	Ref	
	Stage II	67 (50.4)	0.917 (0.217-3.175)	1.94 (1.132-1.4967)	0.354
	Stage III/IV	42 (31.6)	2.913 (1.824-7.308)	3.97 (1.045-14.937)	0.009

a result of formulary restrictions and extremely diverse complexity of therapeutics regimes such as pills burden an dosing frequency. Our study was lower than the study conducted in United Kingdom 34.0%, Brazil 74.3% [24,25]. Due to base line characteristics of the sample composed of patients with follow up in public referral services presented a high proportion of individuals with low income and educational level could contribute with a greater occurrence of non-adherence episodes as these individuals may potential present increased vulnerability and difficulties in accessing the services. The current study was in line with the study conducted in Tanzania 31.6% [26]. Because from all countries in the world those in sub Saharan Africa have the highest rate of HIV/AIDS and non-adherence due to side effects, dosing frequency and route of administration, different opportunistic infections and social stigma.

In our study the mean age of patients were 30-35 years in line with the study conducted in Harar public hospitals [22], Ethiopia which revealed the age of majority respondents were 35 years. This was due to the patients had unprotected sexual intercourse after using alcohol, cigarette and khat which made them to done with copious girls adultery which disclose then HIV/AIDS and at this age patients were not eager to accept the drug due to they believe self-immunity was defeat the infectious disease.

The current survey conducted revealed the magnitude of first line anti-retroviral treatment failure among HIV patients were highest among patient ≥ 42 years were (AOR: 2.04; 95%CI: 1.0761-5.902; P=0.002) 2 times more likely develop treatment failure than other age category were in line with the study carried out in Harare Central Hospital [22] which showed age ≥ 42 years were associated with lower odds of virological failure. This was due to most patients at this age had many co-morbid disease such as dementia, Alzheimer's

which makes the patients not to take his/her pills as recommended through forgetfulness and patients at this age were desperate about life then not had willing to use the medications due to miss understandings.

The recent study regarding marital status divorced (AOR: 1.962; 95%CI: 0.427-2.942; P = 0.008) 2.9 times more likely develop treatment failure than the left marital status was consistent with the study done in Gondar [27] showed being widowed marital status were more likely develop treatment failure. In our survey the divorced was thought about their marital status kaput rather than other marital status, also don't had access things such as cost of transportation, enough eager to take the medication.

Our study showed ART users who dwelled in rural areas were two times more likely to develop first-line ART failure than those reside rural (AOR: 3.51; 95% CI: 1-11.4 30; P = 0.001) 3.5 times more likely develop treatment failure than those in lived in urban. Because those who live in the rural area had no enough information about HIV/AIDS impact and its medication usage value, and also they miss the appointment day due no access facility such as road, unavailability of transportation.

The present survey revealed patients whose baseline WHO clinical stages III/IV (AOR: 3.97; 95%CI: 1.045-14.937; P = 0.009) 3.9 times more likely develop treatment failure than baseline WHO clinical stage I and II in line the study conducted in Ethiopia [28] which showed advanced WHO clinical stage was a significant predictor of ART treatment failure as indicated in studies in Ethiopia. The likelihood of treatment failure was 2.4 times higher among patients in advanced clinical stage III/IV as compared to stage I/II in this meta-analysis. Due to at stages III/IV the patients may bedridden and unable to take the pills unless no aid, and the had several opportunistic infection which perhaps restrict

the patients from oral route of drug administration.

The present study showed HIV/AIDS infected patients who were on AZT + 3TC + NVP (1c) at initial ARV regimen follow up (AOR:2.980; 95%CI: 1.1842-1.749; P = 0.006) 3 times more likely develop treatment failure than those who taken others regimen consistent with study conducted at University of Gondar Referral Hospital [29] which revealed the results of this research showed that initial adult regimens such as D4T + 3TC + EFV(P = 0.007), AZT + 3TC + NVP (P = 0.025), AZT + 3TC + EFV (P = 0.016), TDF + 3TC + EFV (p = 0.009) were significantly protective for treatment failure as compared to regimen AZT + 3TC + NVP. This finding was in line with the study done in Ethiopia. In our survey most patients who taken AZT + 3TC + NVP were interrupt the drug due to the side effects of AZT and NVP which made the patients not comfortable to taken the medication due both medication had severe hepatotoxicity adverse events and headache/dizziness.

Conclusion and Recommendation

The magnitude of first line anti-retroviral treatment failure among HIV patients was high. The initial regimen for HIV/AIDS infected patients were D4T + 3TC + EFV, and majority of patients were substitute the medication none. Side effects were the major reason that why the patients substitute their regimen. Slightly less than half of respondents weren't have diagnosis of recurrent pneumonia (> 2 episodes), and of patients diagnosed not to have antiretroviral treatment failure. Health care workers should have to educate the patients on how the disease where prevented and controlled and government also implement new drafts on the drug efficiency.

Ethical Approval and Considerations

The study protocol was approved by SWAN diagnostic pharmaceutical importer. All participants requiring medical attention and those diagnosed with first line ART failure privacy and behind the scenes were ensured during data collection process. Participant names were not used at the time of data collection and all other personnel information kept anonymously.

Acknowledgments

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