International Journal of HIV/AIDS Prevention, Education and Behavioural Science
2018; 4(2): 44-51
http://www.sciencepublishinggroup.com/j/ijhpebs
doi: 10.11648/j.ijhpebs.20180402.13
ISSN: 2575-5757 (Print); ISSN: 2575-5765 (Online)

Incidence of Virological Failure and Associated Factors among Adult HIV-Positive Patients on First Line Antiretroviral Therapy Regimen, Central Ethiopia

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To cite this article:

Tamrat Endebu, Alem Deksisa, Tibka Moges, Teresa Kisi, Temesgen Ensermu. Incidence of Virological Failure and Associated Factors among Adult HIV-Positive Patients on First Line Antiretroviral Therapy Regimen, Central Ethiopia. *International Journal of HIV/AIDS Prevention, Education and Behavioural Science.* Vol. 4, No. 2, 2018, pp. 44-51. doi: 10.11648/j.ijhpebs.20180402.13

Received: November 10, 2018; **Accepted**: November 28, 2018; **Published**: January 7, 2019

Abstract: Introduction: Viral replication continued to be a major challenge among patients living with HIV and on antiretroviral treatment. In Adama hospital medical college virological failure incidence and factors associated were not well investigated. The aim of this study is to assess Incidence of virological failure and associated factor among adult HIV-patients on first line antiretroviral therapy regimen in Adama Hospital Medical College, Adama town, East Shoa Zone, Oromia Regional State, Ethiopia. Methods: A retrospective cohort study design, 5 years of follow up, was conducted through reviewed and analyzed data of 445 adult patients who had started ART between January 01, 2013 and April 30, 2018. The Kaplan–Meier method was used to estimate the probability of virological failure at different time points. Incidence of virological failure was calculated per 100 Person-years. The Cox proportional hazards model was used to identify factors associated with virological failure. Results: Out of the total 445 cohort patients who were assessed for viral load, there were 40 (9.0%) virological failures in 1,594 person years of retrospective follow-up. This makes the incidence rate of virological failure 2.5 per 100 person-years of follow-up. The cumulative hazard of virological failure at 1 year, 2 years, 3 years, 4 years and 5 years after starting ART amongst those tested was 1.1%, 4.3%, 6.6%, 9.9% and 12.3% respectively. Age 15-24 years [AHR = 4.13, 95%CI (1.29-13.22)], poor adherence [AHR = 2.62, 95%CI (1.21-5.68)], Short duration on ART taking [AHR = 6.93, 95%CI (2.62-18.33)], and changing ART regimen [AHR = 2.82, 95%CI (1.18-6.75)] were risk factors significantly associated with virological failure. Conclusion and recommendations: Overall there was substantial incidence rate of virological failure. Age 15-24 years, poor adherence, and Short duration on ART taking, and changing ART regimen were risk factors significantly associated with virological failure. Therefore, stakeholders should develop strategies and interventions that may help to minimize virological failure by giving more attention to young (15-24 years) age as well as efforts should be strengthened to improve adherence to antiretroviral therapy.

Keywords: Incidence, Virological Failure, Factors, Ethiopia

1. Introduction

The remarkable transformation of HIV into a non-fatal chronic disease was in large part brought by global efforts in making antiretroviral therapy (ART) widely available. Combination ART has unequivocally increased life expectancy and quality among infected people worldwide

[1]. Ethiopia has adopted the UNAIDS90-90-90 treatment target by 2020[2] in which the country has planned to reach 90% of viral suppression among all people receiving antiretroviral treatment [3,4]. However, as the use of HAART increases, the issue of drug resistance and subsequent treatment failure presenting as one or more of clinical, immunological and virological failure (VF) appears as a challenge [5-8].

After ART initiation, patients are monitored for their treatment response clinically, immunologically and virological. At this time viral load monitoring has become the standard of care to monitoring the success and diagnosing of antiretroviral treatment. Thus, the world health organization recommends routine annual viral load monitoring for all patients, on antiretroviral therapy as the most accurate and available measure of effective treatment response [9].

An elevated or 'non-suppressed' VL (>1000 copies/ml) in a patient who has been on ART for at least six months can indicate either therapeutic failure due to antiretroviral resistance, and/or poor adherence to treatment. To distinguish between these two conditions, a patient with an elevated VL should receive adherence support followed by retesting three to six months later [1, 10]. According to the WHO guidelines, patients whose VLs are not suppressed at retesting can be classified as having 'virologic failure' [9].

Current guidelines recommend that once patients start treatment, virological failure should not exceed 10% [10]. However, studies show that different incidence of virological failure and viral replication continues to be a major challenge among patients living with HIV, with emerging drug resistance and subsequent treatment concern for HIV programs in resource-limited settings where treatment options are limited [11]. Although different cutoff points are used to define virologic failure, studies from China showed virological failure of 12% [12], from South Africa failure rate of 4.5 per 100 person years follow up (PYFU)[13], from Indian virological failure 10.7 per 100 person-years of observation [5]. In Myanmar the incidence rate of virological failure after first-line ART amongst those tested was 3.2 per 100 person-years of follow-up (PYFU) [7]. In resource-limited settings that studies done using virological criteria to define failure, the failure rate per 100 patient years of follow-up was, 7.10 in Africa, and 2.55 in Asia [11]. Virologic failure were associated with predictors such as ART adherence, alcohol consumption, age, lack of disclosure, and opportunistic infections during initiation of ART [14-17].

Data on viral load monitoring is one of the key WHO reportable indicators that should be periodically reported to continuously evaluate the success of ART programs [1]. Hence, earlier detection of virological failure allows both targeted adherence interventions and better preservation of efficacy of second-lineregimens and maintaining low viral loads, partners and children be protected from horizontal and vertical transmission. Patients also are protects from the progression to AIDS and associated co infections. However, there is paucity of information in the virologic status and its predictors. This study aimed to describe incidence of virological failure and associated factor among adult HIV/AIDS patients on first line antiretroviral therapy regimen in Adama Hospital Medical College. Examination of these data helps to identify the challenges that must be overcome in ensuring high treatment success rate and the viral load suppression in realizing the 90-90-90 treatment targets.

2. Methods

2.1. Study Design and Setting

Hospital based retrospective cohort study design was conducted in Adama hospital medical college, which is located in Adama special zone at Oromia regional state, 99km away from Addis Ababa the capital of Ethiopia. The hospital serves around 3,000, 000-people from different parts of Oromia region and other nearby region. The hospital runs both inpatient and outpatient treatment activities, with bed capacity of 219, HIV care and treatment clinic is one of the core part of outpatient activities, The chronic HIV care clinic was launched in 2003 and it is one of the first three hospitals in Oromia that started providing free ART in 2005 . The service it is providing to Adult and Pediatric ART, Currently it is serves more than 10thousand patients, of whom about 6049are on ART. More than two thirds of these patients are on first line regimes.

2.1.1. Study Population

Study population was randomly selected the medical records of HIV positive adult who have been enrolled on ART between January 1, 2014 and April 31, 2018.

2.1.2. Study Subjects

The study included all HIV-infected adults aged 15 years or older who had been on ART for at least 12 months. In this study, virologic failure was defined based on the recent WHO guidelines as two consecutive VLs > 1000 copies/ml detected within 12 months while on ART (18).

2.2. Sample Size Determination

Sample size was determined using Epi Info™ Version: 7.2.1.0 StatCalc by considering 95 % confidence level, 80 % power, unexposed to exposed group ratio of one and taking the key predictor of virological failure (age <35 years) from a previous study (14). Therefore, the calculated sample size was 224. However, to improve the power of the study we increased the sample size close to double (445 total sample size) was analyzed.

2.3. Data Collection and Analysis

Data was extracted from patient charts using a pretested structured data extraction format. Accordingly, all charts containing detailed information about patients who had at least twelve month of follow up were on HAART from January 1, 2013to April 30, 2018 was reviewed. Six health professionals trained for 2 days collected the data. The principal investigator and the supervisor closely monitoring

the whole data collection process on a daily basis.

Data has entered into Epi Info version 7.2.1 and analyzed using SPSS version 21. Descriptive statistics, including mean values and frequencies, was used describe demographic, clinical, hematologic, and medication-related characteristics of patients. . The Kaplan–Meier method was used to estimate the probability of virological failure at different time points. Incidence of virological failure was calculated per 100 Person-years of observation. The Cox proportional hazards model was used to identify predictors associated with virological failure.

Ethical clearance was obtained from Adama General Hospital medical college of Institutional Review Board (IRB). Following the approval, Official letter of co-operation has been written to concerned bodies by Adama General Hospital medical college and Permission has been granted from Oromia Regional Health Bureau and Adama Hospital Medical College. As the study was conducted through review of medical cards, the individual patients is not exposed to any as far as the confidentiality maintained. Moreover, no personal identifier was used on data collection form.

3. Results

Socio-demographic baseline characteristics

The study, cohort population comprised 445 adults initiating ART between January 01, 2013 and April 30, 2018. They were followed up for a total of 1594 person-years. Of these, 58.9% of cohort was female. The mean (+SD) age of cohort at ART initiation was 35.92 ±10.06 years. Around one tenth of the study cohort, 53(11.9%) were age 15-24 years old, around two fifth, 169(38.0%) were age 25-34 years, around one third, 125(28.1%) were age 35-44 years and about one quarter 98(22.0%) were age equal or greater than 45 years. Regarding the origin of patient address, three fourth, 341(76.6%) were attend the hospital from its catchment area while the rest were from out of the catchment. Nearly two third, 296(66.5%) were Orthodox, around one fifth, 81(18.2%) were Muslim and one tenth were protestant religion followers. Regarding the marital status, about half, 217(48.8%) were married, 90(20.2%) were single, 85(19.1%) were divorced and around one tenth, 53(11.9%) were widowed. Around one fifth of the study subjects, 83(18.7%) were illiterate, 19(4.3%) were able to read and write, about two fifth, 154(36.9%) were elementary educated, about one third, 128(28.8%) were high school and around one tenth, 51(11.5%) were educated diploma and above (Table 1).

Table 1. *Socio-demographic baseline characteristics among adult HIV-patients on first line ART regimen in AHMC, Adama town, East Shoa Zone, Oromia Regional State, Ethiopia from January 01, 2013 to April 30, 2018.*

Variables		Frequency	Percent
Sex			
	Female	262	58.9%
	Male	183	41.1%
Age category			
	15-24	53	11.9%
	25-34	169	38.0%
	35-44	125	28.1%
	>=45	98	22.0%
Origin of address			
	Within catchment	341	76.6%
	Out of the catchment	104	23.4%
Religion			
	Orthodox	296	66.5%
	Muslim	81	18.2%
	Protestant	49	11.0%
	Catholic	10	2.2%
	Other	9	2.0%
Marital status			
	Single	90	20.2%
	Married	217	48.8%
	Divorced	85	19.1%
	Widowed	53	11.9%
Education			
	Illiterate	83	18.7%
	read and write	19	4.3%
	elementary school	164	36.9%
	high school	128	28.8%
	diploma and above	51	11.5%
Occupation			
	employed by government	62	13.9%
	self employed	106	23.8%
	Jobless	113	25.4%
	Student	24	5.4%
	Other	140	31.5%

Patient clinical characteristics

Out of the total cohort almost all, 426(95.7%) were disclosed their HIV status to at least one person other than their health providers. Around four fifth of the cohort, 364(81.8%) had BMI greater than 18. Almost all, 439(98.7%) had working functional status. Around nine tenth of cohort, 404(90.8%) had good adherence status whereas one tenth, 41(9.2%) had poor adherence status. About one third of the cohort, 34(7.6%) were changed/made ART regimen modification. Around quarter of cohort, 98(22.0%) had 12-23 months of duration on ART, 83(18.7%) had 24-35 months of duration on ART and around one third, 145(32.6%) had duration on ART greater or equal to 45 months. Slightly near to one tenth of cohort, 32(7.2%) were interrupted their follow up on ART. Regarding of the baseline CD4 count, about one third, 158(35.5%) had CD4 count less than 200 cell/μ, 127(28.5%) had 200-300 cell/μ and 160(36.0%) had CD4 count greater than 300 cell/μ. Majority of the cohort, 374(84.0%) had been taking TDF+3TC+EFV first line treatment (Table 2).

Table 2. *Clinical characteristics among adult HIV-patients on first line ART regimen in AHMC, Adama town, East Shoa Zone, Oromia Regional State, Ethiopia from January 01, 2013 to April 30, 2018.*

Variables		Frequency	Percent
Disclosure status			
	No	19	4.3%
	Yes	426	95.7%
Body Mass Index			
	<16 BMI	16	3.6%
	16- 18 BMI	65	14.6%
	> 18 BMI	364	81.8%
Functional status			
	Working	439	98.7%
	Ambulatory/Bedridden	6	1.3%
Adherence			
	Good	404	90.8%
	Poor	41	9.2%
ART regimen changed			
	No	411	92.4%
	Yes	34	7.6%
Duration on ART (Months)			
	12-23	98	22.0%
	24-35	83	18.7%
	36-48	119	26.7%
	>48	145	32.6%
On ART interrupted			
	Yes	32	7.2%
	No	413	92.8%
Base line CD4 count(cells/μ)			
	< 200	158	35.5%
	200-300	127	28.5%
	> 300	160	36.0%
CurrentARTregimen			
	AZT,3TC, NVP(1c)	24	5.4%
	AZT,3TC, EFV (1d)	20	4.5%
	TDF,3TC, EFV (1e)	374	84.0%
	TDF,3TC, NVP (1f)	15	3.4%
	Other	12	2.7%

Incidence of virological failure

Out of the total 445 cohort patients who were assessed for viral load, there were 40 (9.0%) virological failures in 1,594 person years of retrospective follow-up (PYFU). This makes the incidence rate of virological failure 2.5 per 100 person-years of follow-up. The cumulative hazard of virological failure at 1 year, 2 years, 3 years, 4 years and 5 years after starting ART amongst those tested was 1.1%, 4.3%, 6.6%, 9.9% and 12.3% respectively (Figure 1).

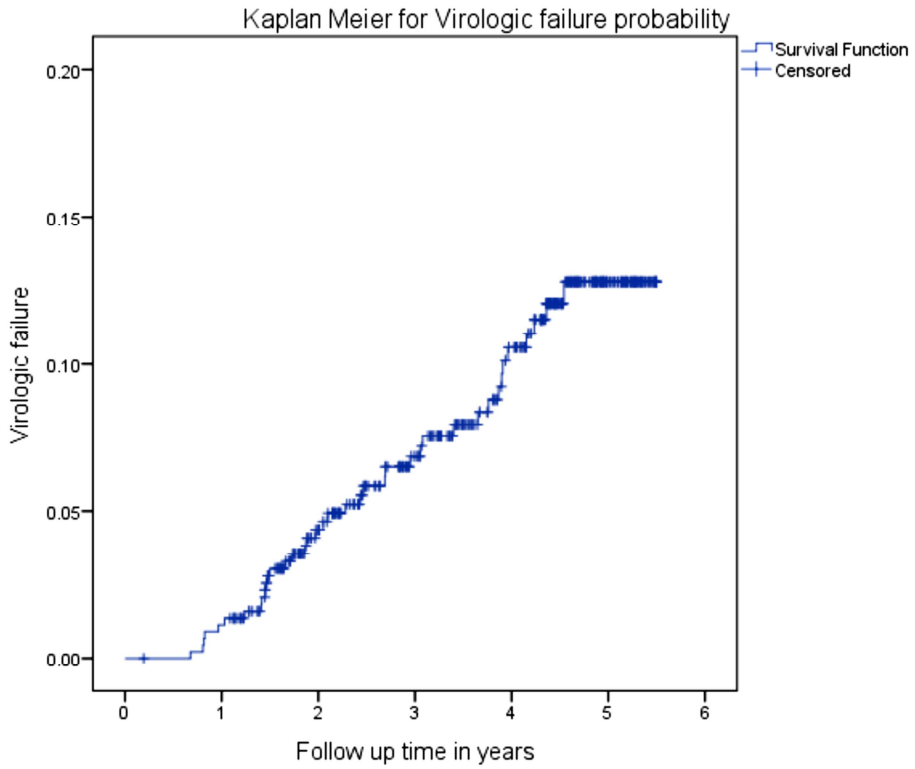

Figure 1. *Cumulative incidence of virologival failure among adult HIV/AIDS patients on first line ART regimen in AHMC, Adama town, East Shoa Zone, Oromia Regional State, Ethiopia from January 01, 2013 to April 30, 2018.*

Risk factors of virological failure

Bivariate and multivariate analysis was conducted to determine predictors of virological failure. At bivariate level, age, marital status, adherence status, base line CD4 count (cells/μ), duration on ART in months, Interrupted follow up on ART and changing ART regimen were significantly associated(p-value less than 0.05) factorswith virological failure. All of the variables with p-value less than 0.25 at bivariate analysis were incorporated in the final multivariable model. After adjusting for covariates, age, adherence, duration on ART and changing ART regimen were predictors significantly associated with the risk of virological failure.

The risk was four times higher among patients of age from 15-24 as compared to those age equal or greater than 45 years with adjusted hazard ratio [(AHR) = 4.13, 95%CI (1.29-13.22)]. The risk of virological failure was about three times higher among patients those had poor adherence with treatment as compared to those had good adherence [AHR = 2.62, 95%CI (1.21-5.68)]. Patients those had duration of 12-23 months on ART were seven times higher risk of virological failure as compared to those patients had duration of greater than 45 months on ART [AHR = 6.93, 95%CI (2.62-18.33)]. The risk of virological failure was about three times higher amongst patients those changed ART regimenas compared to those did not change ART regimen [AHR = 2.82, 95%CI (1.18-6.75)](Table 3).

Table 3. *Risk factors associated with Virological failure among adult HIV/AIDS patients on first line ART regimen in AHMC, Adama town, East Shoa Zone, Oromia Regional State, Ethiopia from January 01, 2013 to April 30, 2018.*

Characteristics	Number (N)	Number of VF	Crude HR 95% CI	P-Value	Adjusted HR 95% CI	P-Value
Total	445 (100%)	40 (9.0%)				
Age at ART started						
15-24	53 11.9)	13(32.5)	4.40(1.66-11.65)	0.003	4.13(1.29-13.22)	0.017
25-34	169(38.0)	18(45.0)	1.75(0.69-4.42)	0.234	1.86(0.71-4.86)	0.207
35-44	125(28.1)	3(7.5)	0.41(0.10-1.66)	0.212	0.59(0.15-2.44)	0.469
>=45	98(22.0)	6(15.0)	1.00		1.00	
Marital status						
Single	90(20.2)	15(37.5)	4.60(1.05-20.17)	0.043	1.31(0.25-6.72)	0.749
Married	217(48.8)	17(42.5)	2.15(0.50-9.29)	0.307	1.74(0.38-8.02)	0.479
Divorced	85(19.1)	6(15.0)	1.69(0.34-8.37)	0.523	1.13(0.21-5.99)	0.887
Widowed	53(11.9)	2 (5.0)	1.00		1.00	
Adherence						
Good	404(90.8)	30(75.0)	1.00		1.00	
Poor	41(9.2)	10(25.0)	3.25(1.59-6.68)	0.001	2.62(1.21-5.68)	0.015
Base line CD4 count (cells/μ)						
<200	158(35.5)	22(55.0)	1.96(0.92-4.14)	0.079	2.10(0.94-4.69)	0.069

Characteristics	Number (N)	Number of VF	Crude HR 95% CI	P-Value	Adjusted HR 95% CI	P-Value
200-300	127(28.5)	8(20.0)	0.80(0.32-2.04)	0.640	0.84(0.31-2.30)	0.740
>300	160(36.0)	10(25.0)	1.00		1.00	
Duration on ART (months)						
12-23	98(22.0)	13(32.5)	6.62(2.79-15.66)	0.001	6.93(2.62-18.33)	0.001
24-35	83(18.7)	9(22.5)	2.79(1.13-6.90)	0.026	2.48(0.86-7.18)	0.094
36-48	119(26.7)	6(15.0)	0.85(.31-2.32)	0.753	0.94(0.33-2.69)	0.902
>48	145(32.6)	12(30.))	1.00		1.00	
On ART Interrupted						
Yes	32(7.2)	8(20.0)	3.39(1.56-7.37)	0.002	1.32(0.53-3.31)	0.555
No	413(92.8)	32(80.0)	1.00		1.00	
ART regimen changed						
No	411(92.4)	30(75.0)	1.00		1.00	
Yes	34(7.6)	10(25.0)	3.95(1.91-8.17)	0.001	2.82(1.18-6.75)	0.020

Note that 'black *' indicated significantly associated at bivariate level and 'black **' significantly associated at multivariate level

4. Discussion

Key findings from this study showed, overall incidence rate of virological failure was 2.5 per 100 person years follow up (PYFU). The 5 year cumulative incidence of failing after starting ART amongst those tested was 12.3%. Age, adherence, duration on ART and changing ART regimen were factors significantly associated with the risk of virological failure.

This study shows that the virological failure rate was 2.5 per 100 PYFU. The cumulative incidence of failing at 5 years after starting ART was 12.3%. This finding was similar with studies from China(12%failed after 2 years on ART)(12). But, it was lower than studies from India (10.7 failures per 100 PYFU and cumulative failure incidence of 16.5% over 2 years)(5), Myanmar (3.2 per 100 PYFU)(7), and from South Africa (failure rate of 4.5 per 100 PYFU)(13). The discrepancy might be due to different viral load cut-off points, duration of time on ART and follow-up periods.

The risk of virological failure was four times higher among patients of age from 15-24 as compared to those age equal or greater than 45 years [AHR = 4.13, 95%CI (1.29-13.22)]. This finding was supported by study from India(5), Uganda(15), Kenya (19) , Cameroon (20), Mozambique(21), France (22) and Addis Ababa (23). This might be due to differences in lifestyles, as most of the younger adults commonly suffered from less healthy personality traits and were more vulnerable to substance abuse. Moreover, they had less emotional stability to cope with the social stigma, discrimination, and the adverse consequences of the disease itself. This suggests that depression, anxiety, and unhealthy behaviors could negatively affect dietary intake and treatment outcomes of clients (24).

The risk of virological failure was about three times higher among patients those had poor adherence with treatment as compared to those had good adherence [AHR = 2.62, 95%CI (1.21-5.68)]. This finding was supported by study from India(5), Africa (25), Gondar, Northwest Ethiopia (26), Mozambique(21), France (22), and China (16). This is due to the evident that individuals missing 3 doses of ART per month are associated with an increased risk of drug resistance and reduced immunity (27) This results in the loss of the opportunity to suppress viral replication and leads to virological failure (10).

Patients those had duration of 12-23 months on ART were seven times higher risk of virological failure as compared to those patients had duration of greater than 45 months on ART [AHR = 6.93, 95%CI (2.62-18.33)]. This study finding was consistent with study from Gondar, Northwest Ethiopia (26), and contradict with studies Gabon (28), Swaziland (29) and Mozambique (21). The possible reason might be that at initiation of ART drug, the likelihood of developing drug interruption and poor adherence might be increased which might have led to virological failure.

The risk of virological failure was about three times higher amongst patients those changed ART regimenas compared to those did not change ART regimen [AHR = 2.82, 95%CI (1.18-6.75)]. This finding was supported with study from Myanmar(7). This might be due to patient clinical background/condition that may force to change the regimen.

Limitations: Baseline viral load testing is not routinely done in this setting. It would have been important to examine the association between baseline viral load and risk of virological failure. In addition, some other important variables like patient behavior and other were not included.

5. Conclusion

This study shows there was substantial incidence rate of virological failure (2.5 per 100 PYFU and the 5 years cumulative incidence of failing after starting ART amongst those tested was high (12.3%). This study also showed that age 15-24 years, poor adherence, short duration on ART taking, and changing ART regimen were risk factors significantly associated with virological failure. Therefore, targeted HIV care interventions shall be provided to young (15-24 years) ages and efforts should be strengthened to enhance adherence to ART, which helps to boost immunity and suppress viral replication and load.

List of Acronyms

ARTAntiretroviral Therapy
AIDS Acquired Immune Deficiency syndrome
FMOH Federal Ministry Of Health
HAARTHighly Active Anti Retroviral Therapy

HIVHuman Immune Deficiency Virus

NNRTINon-Nucleoside Reverse Transcriptase Inhibitor

NRTINucleoside or Nucleotide Reverse Transcriptase Inhibitor

PYFUPatient Years of Follow-Up

USAIDUnited States Agency for International Development

VLViral Load

WHOWorld Health Organization

Competing Interests

There is no any competing interest among the authors.

Author's Contributions

ET, DA and MT were involved in the design and conception of the study; the analysis and interpretation of the findings. DA, ET, MT, KT and ET: involved in analysis, interpretation and writes up of the manuscript. All the authors read and approved the final content of the manuscript.

Acknowledgements

The Authors gratefully acknowledge all the participants and data collectors. The authors acknowledge AHMC department chairs for their general support.

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References

[1] World health organization Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection/recommendations for a public health approach second edition, 2016. http://www.who.int/hiv/pub/arv/arv-2016/en/.

[2] UNAIDS.90–90-90:. An ambitious treatment target to help end the AIDS epidemic. In. October,2014 ed. http://www.unaids.org/sites/default/files/ media_asset/90-90-90_en_0.pdf (accessed 5 Apr 2015). 2014.

[3] Federal HIV/AIDS Prevention and Control OfficeHIV/AIDS strategic plan 2015-2020 in an investment case approach, Addis Ababa (Ethiopia): Federal HIV/AIDS Prevention and Control Office. 2014, 63 p. https://hivhealthclearinghouse.unesco.org/library/documents/hivaids-strategic-plan-2015-2020-investment-case-approach.

[4] Ethiopia, Country/Regional Operational Plan (COP/ROP) Strategic Direction Summary 2017. https://www.pepfar.gov/documents/organization/272012.pdf.

[5] Anita Shet, Ayesha De Costa Virological efficacy with first-line antiretroviral treatment in India: predictors of viral failure and evidence of viral re suppression Tropical Medicine and International Health, 2015 doi:10.1111 /tmi.12563/volume 20.

[6] Billong SC, Fokam J, Aghokeng AF, Milenge P, Kembou E, Abessouguie I, et al. Population-based monitoring of emerging HIV-1 drug resistance on antiretroviral therapy and associated factors in sentinel site in Cameroon: low levels of resistance but poor program maticpeformance. Plo Sone. 2013;8 (8): e72680.Epub2013/08/31.doi:10.1371/journal.pone.0072680PMID:23991142.

[7] Kyaw NTT, Harries AD, Kumar AMV, OoMM, Kyaw KWY, Win T, et al. (2017) High rate of virological failure and low rate of switching to second-line treatment among adolescents and adults living with HIV on first-line ART in Myanmar, 2005-2015. PLoS ONE 12(2): e0171780.doi:10.1371/journal.

[8] Liégeois F, Vella C, Eymard-Duvernay S, et al. Virological failurerates and HIV-1 drug resistance patterns in patients on first-lineantiretroviral treatment in semirural and rural Gabon. J Int AIDS Soc.2012;15(2):17985Liégeois F, Vella C, Eymard-Duvernay S, et al. Virological failurerates and HIV-1 drug resistance patterns in patients on first-lineantiretroviral treatment in semirural and rural Gabon. J Int AIDS Soc.2012;15(2):17985.

[9] World Health Organization (2013) Global update on HIV treatment: Results, impact and opportunities. http://www.who.int/about/licensing/copyright_form/ en/index.html).

[10] Federal Ministry of Health.(2014) National Guidelines for comprehensive HIV prevention care and treatment, Ethiopia, 2014.

[11] Roberts T, Bygrave H, Fajardo E, Ford N. Challenges and opportunities for the implementation of virological testing in Resource -limited settings. J Int AIDS Soc 2012; 15:17324.

[12] Ma Y, Zhao D, Yu L, Bulterys M, Robinson ML, Zhao Y, et al. Predictors of virologic failure in HIV-1-infected adults receiving first-line antiretroviral therapy in 8 provinces in China. ClinInfect Dis. 2010; 50 (2):2 64±271. doi: 10.1086/649215PMID:20017637.

[13] Fox MP, Cutsem GV, Giddy J, Maskew M, Keiser O, Prozesky H, et al. Rates and predictors of failure of first-line antiretroviral therapy and switch to second-line ART in South Africa. JAcquir Immune Defic Syndr. 2012; 60(4):428±437.doi:10.1097/QAI.0b013e3182557785PMID:22433846.

[14] Bayu B, Tariku A, Bulti AB, Habitu YA, Derso T, Teshome DF Determinants of virological failure among patients on highly active antiretroviral therapy in University of Gondar Referral Hospital, Northwest Ethiopia: a case–control study HIV/AIDS - Research and Palliative Care » Volume 9 2017:9 Pages 153—159; DOI https://doi.org/10.2147/HIV.S139516.

[15] Kazooba P, Nsubuga B, Mayanja, Levin J, Masiira B, Pontiano Kaleebu P. Virological failure on first-line antiretroviral therapy; associated factors and a pragmatic approach for switching to second line therapy–evidence from a prospective cohort study in rural South-Western Uganda, 2004-2011: Pan African Medical Journal. 2018;29:191. doi:10.11604/pamj.2018.29.191.11940.

[16] Zuo Z, Liang S, Sun X, Bussell S, Yan J, Kan W, et al. (2016) Drug Resistance and. Virological Failure among HIV-Infected Patients after a Decade of Antiretroviral Treatment Expansion in Eight Provinces of China. PLoS ONE11(12): e0166661. doi:10.1371/journal.

[17] Sisay MM, Ayele TA, Gelaw YA, Tsegaye T, Gelaye KA and Melak MFIncidence and risk factors of frst-line antiretroviral treatment failure among human immunodefciency virus-infected children in Amhara regional state, Ethiopia: a retrospective follow-up study. BMJ Open 2018;8:e019181. doi:10.1136/bmjopen-2017-019181.

[18] WHO. HIV/AIDS:. Monitoring response to ART and diagnosis of treatment failure. In. June, 2013 ed. http://www.who.int/hiv/pub/guidelines/arv2013/ art/artmonitoring/en/ (Accessed 31 May 2016); 2013.

[19] Sang RKA, Miruka FO. Factors associated with virologic failureamongst adults on antiretroviral therapy in Nyanza Region, Kenya. IOSR J Dent Med Sci. 2016;15(7):108–121.

[20] Meriki HD, Tufon KA, Afegenwi MH, et al. Immuno-haematologicand virologic responses and predictors of virologic failure in HIV-1infected adults on first-line antiretroviral therapy in Cameroon. InfectDis Poverty. 2014;3:5.

[21] Rupérez M, Pou C, Maculuve S, et al. Determinants of virologicalfailure and antiretroviral drug resistance in Mozambique. J Antimicrob Chemother. 2015;70(9):2639–2647.

[22] Parienti JJ, Massari VR, Descamps D, et al. Predictors of virologic failure and resistance in HIV-infected patients treated withnevirapine- or efavirenz-based antiretroviral therapy. Clin Infect Dis.2004;38(9):1311–1316.

[23] Tigist Bacha, Birkneh Tilahun, and Alemayehu Worku, Predictors of treatment failure and time to detection and switching in HIV-infected Ethiopian children receiving first line anti-retroviral therapy BMC Infectious Diseases2012,12:197, http://www.biomedcentral.com/1471-2334/12/197.

[24] Rabkin JG. HIV and depression: 2008 review and update. Behav Aspects HIV Manag. 2008;5(4):163–171.

[25] Charles M. Kwobah, Ann W. Mwangi et al,. Factors Associated with First-Line Antiretroviral TherapyFailure amongst HIV-Infected African Patients:A Case-Control Study, World Journal of AIDS, 2012, 2, 271-278http://dx.doi.org/10.4236/wja.2012.24036.

[26] Bayu. B, Tariku. A, Balcha. A, Ayanaw. Y, Fetene. D. (201) Determinants of virological failure among patients on highly active antiretroviral therapy in University of Gondar Referral Hospital, Northwest Ethiopia press journal: HIV/AIDS-Research and palliative care 8 August 2017978-92-4-15500.

[27] AIDSinfo. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. 2016.

[28] Liégeois F, Vella C, Eymard-Duvernay S, et al. Virological failurerates and HIV-1 drug resistance patterns in patients on first-lineantiretroviral treatment in semirural and rural Gabon. J Int AIDS Soc.2012;15(2):17985Liégeois F, Vella C, Eymard-Duvernay S, et al. Virological failurerates and HIV-1 drug resistance patterns in patients on first-lineantiretroviral treatment in semirural and rural Gabon. J Int AIDS Soc.2012; 15(2):17985.

[29] Jobanputra K, Parker LA, Azih C, et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. PLoS One. 2015; 10(2):e0116144.