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# A Comparison of Patients on First Line and Second Line Antiretroviral Therapy in Dar es Salaam, Tanzania

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**Abstract**

***Background***
Understanding characteristics of patients on second-line antiretroviral therapy (ART) in comparison to patients on first-line ART is important in addressing demographic and clinical issues related to treatment failure.

***Broad objective***
We aimed to compare characteristics of patients on second line ART to those of patients on first line ART and to assess factors associated with second line ART treatment in Dar es Salaam, Tanzania.

***Methodology***
Adult patients were systematically recruited in a cross sectional study from one primary level and one secondary level HIV clinics in Dar es Salaam Tanzania. Participants' socio-demographic and clinical characteristics were recorded. Medians and interquartile ranges were used to compare continuous variables while proportions were used to compare categorical variables. Logistic regression was used to determine factors associated with second line ART treatment.

***Results***
We recruited 102 patients from each clinic. Compared to patients on 1st line ART, significantly more patients on second line ART were employed; 90.2% vs. 72.5%, p=0.001, had been on ART for ≥60 months, 71.6% vs. 33.3%, p<0.001, had changed ART regimen ≥3 times, 16.7% vs. 3.9%, p=0.003, presented with lower median (IQR) pre-ART CD4 counts 72 (26-192) vs. 150 (61-273) cells/µL respectively, p=0.03, had lower median (IQR) CD4 counts at the time of the study, 326(213-412) vs. 422 (299-583) cells/µL, p<0.001, had higher median (IQR) Creatinine; 0.9 (0.75-1.2) vs. 0.78 (0.66-0.9) mg/dl, p<0.001. Employment and being on ART for >60months were 2.5 and 4.4 times respectively more likely seen in patients on second line ART compared to first line ART, p<0.05.

***Conclusion and recommendation***
Majority of patients on second-line ART initiated ART with very low CD4 counts, had been on ART for more than sixty months and had changed their ART three times or more. They also had lower CD4 counts at the time of the study. Employment and duration of ART predicted likelihood of being on second-line ART. We recommend early screening for HIV and ART initiation before the immunity is severely compromised in order to reduce the burden of HIV treatment failure.

***Key words:*** *First line antiretroviral therapy, Second line antiretroviral therapy, antiretroviral therapy resistance, HIV patients' characteristics, Tanzania, ART adherence.*

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**Introduction**

Antiretroviral Therapy (ART) has transformed Human Immunodeficiency Virus (HIV) infection from a fatal to a chronic disease(1). In pre-ART era the median survival from the time of AIDS diagnosis was 12 months. The advent of ART has significantly improved survival rates(Palella *et al.*, 1998; Crummy *et al*, 2008; Trickey *et al.*, 2017). Estimates suggest that by 2006 approximately 85–90% of patients survived beyond 6 years after the diagnosis of AIDS (5).The current test and treat approach has great promises for survival as patients are treated when their immunity is still high. An HIV infected person is said to have an improved survival (6) that the life expectancy is comparable to that of the general population(7) provided ART is initiated before they are severely immunosuppressed.

ART has successfully brought down both the incidence and prevalence of HIV associated Tuberculosis (TB)(8). The pre-ART rates of tuberculosis, esophageal candidiasis, invasive bacterial infections, *pneumocystis jirovecii*, varicela zoster, herpes simplex, cerebral and ocular toxoplasmosis, cytomegaloviral infections have been significantly brought down with the advent of ART(9). With the exception of invasive cervical carcinoma, the risks for AIDS-related malignancies like Kaposi's sarcoma, primary central nervous system (CNS) lymphoma and non-Hodgkin lymphoma have been significantly decreased by ART(10). However, AIDS defining and non-AIDS defining malignancies continue to be more prevalent even in treated HIV-infected persons than in the general population(11).
Apart from decreasing morbidity and mortality, the scale up of antiretroviral therapy (ART) has also been associated with reduced HIV acquisition and/or transmission with a resultant increased life expectancy in certain parts of Sub-Saharan Africa(12).

HIV mutations are a drawback in HIV management as they result into ART resistance. ART resistance is largely due to poor adherence to ART (13–15). Other factors which are associated with ART resistance include low pre-ART CD4 counts below 200 cells/µl (16,17) high pre-ART viral load of ≥ 1000 copies /ml, being on ART for more than 24 months (17), discontinuation of ART, persistent diarrhea, frequent eating of a diet containing wheat or barley(18). HIV treatment failure is trifurcated into virological, immunological and clinical failure. The presence of viral load above 1000 copies/ml in two consecutive viral load measurements after 3 months of adherence support depicts virologic failure. Immunological failure is when the CD4 count falls to the baseline or below baseline or persistent CD4 levels below 100 cells/mm3 for adult and adolescent or below 200

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cells/mm$^3$ in children younger than 5 years. Clinical failure is when there is an occurrence or recurrence of advanced WHO clinical stage after 6 months of therapy(19). Treatment failure to first line ART is uncalled for. In developing countries, many of HIV programs cannot switch treatment beyond second line due to economical constrains. Sixteen years after universal ART provision to HIV infected patients in Tanzania beginning in the year 2004, ART drug resistance is already rampant in the country (15,17,20). Among adults, a cohort study in Tanzania found virology failure in up to 15% with drug resistance mutations seen in over three quarters (15). One way to minimize treatment failure and switching drugs to second line is to understand factors surrounding treatment switching, particularly patients' characteristics. We conducted this study aiming at describing the characteristics of patients already on second line ART in Dar es Salaam and determining factors associated with second line ART treatment. Prevalence of some of the known risk factors for treatment failure was determined and compared their rates to those of patients still on first line ART. We believe understanding these factors enlightens on future preventive strategies for treatment failure.

## Methods

### *Design and setting of the study*

The study was a hospital based descriptive comparative cross-sectional study among patients attending urban care and treatment clinics (CTC) in Dar es salaam. Data collection was done from March 2014 to September 2014.

The study was conducted in two clinics; a secondary level clinic Amtulabhai Karimjee Care and Treatment Clinic (CTC) which attended patients on second line ART and a primary level clinic Amana CTC where patients on first line were obtained. Amtulabhai Karimjee Clinic (AKC) is a Care and Treatment clinic in Ilala municipality supported by HARVARD-PEPFAR collaborative services. This clinic catered for all patients with treatment failure referred from various HIV clinics within the 3 municipal hospitals as well as all the healthcare centers that provided HIV care and treatment within Dar es Salaam. The AKC had enrolled around 2000 patients who were diagnosed with HIV treatment failure and were currently on second-line ART. On a clinic day an average of 40 patients attended the clinic.

Amana hospital is one of the three municipal hospitals in Dar-es-salaam. It is a public hospital serving patients from Ilala municipality. All HIV treatment failure cases from Amana

got transferred to AKC for second line HIV treatment. Amana CTC had enrolled about 16,000 HIV infected patients. An average of 200 patients was seen on a single clinic day. Both AKC and Amana CTC offered services five days a week. In both clinics, the very sick patients were given monthly follow up clinics while stable patients and those with undetectable viral load were given 2 monthly or three monthly follow up clinics.

***Study population***

Participants comprised of adult HIV infected patients who were on second-line ART who attended Amtulabhai Karimjee CTC and those on first-line ART who attended Amana CTC. Patients on first-line medications used nucleoside analogue reverse transcriptase inhibitors (NRTIs) such as Zidovudine (AZT), Lamivudine (3TC), Abacavir (ABC), Emtricitabine (FTC), and Stavudine (d4T) in different combinations with non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) Nevirapine (NVP) and Efavirenz (EFV) or nucleotide analogue Tenofovir (TDF). These combinations were AZT+ 3TC+EFV, AZT+3TC+NVP, TDF+FTC+EFV, TDF+FTC +NVP, TDF+3TC+EFV, TDF+3TC+NVP, d4T+3TC+NVP and d4T+3TC+EFV.

For the second-line ART patients used a combination of NRTIs or nucleotide analogues and Protease inhibitors (PIs) such as Lopinavir boosted by Ritonavir ((LPV/r) and Atazanavir boosted by Ritonavir (ATV/r). The choice of the drug combination depended on the first line regimen that the patient was on. Second line combinations used were TDF+3TC or FTC +LPV/r or ATV/r, AZT + 3TC + LPV/r or ATV/r, ABC + 3TC + LPV/r or ATV/r.

***Data collection procedure***

Consented HIV infected patients aged 18 years or older who were on second-line ART in Amtulabhai Karimjee CTC and those on first-line ART at Amana CTC were recruited into the study. Patients' recruitment was done systematically in every Wednesday (Amana CTC) and every Thursday (AKC). Every 5$^{th}$ patient at AKC and every 40$^{th}$ patient at Amana were recruited until the calculated sample size of 102 for each clinic was achieved. The sampling frame based on the patients who attended the clinic on the specified days. If a patient declined participation, the next patient on the list was invited. An average total of 5 to 8 patients were recruited per day from each clinic.

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A pre-tested structured questionnaire was used to collect socio-demographic, clinical and laboratory data. Care and treatment cards number 2 (CTC 2 cards) were used to obtain baseline and current CD4 counts and duration of ART use. Most of the laboratory data were obtained from the patients' files. There was inconsistence in availability of viral load (VL) records thus very few patients had a record on viral load, as such VL data was not analyzed. We also compared CD4 cell counts at the time of the study. This was CD4 cell counts that were done within one month of data collection date. For patients whose laboratory results did not meet the above criteria, their blood was taken and tested during the time of the study. For CD4 counts and Full blood count 5mls of blood was put in tubes containing an anticoagulant EDTA. Analysis of the CD4+ T lymphocyte cell counts at the time of the study was done using flow cytometry using Becton Dickson Facs count machine while FBC was done using an automated counter Cell Dyn System 1200 (Abbott Diagnostics division). Blood for biochemical analysis of alanine aminotransferase (ALAT) and serum createnine was put in a vacuttainer that did not contain EDTA and analyzed using direct spectrophotometric measurement using an automated machine (Cobas Integra 400 Plus analyzer, Roche, Germany).

***Statistical analysis***

Data were entered into a statistical package for social sciences (SPSS) version 21 for analysis. Medians and interquartile ranges were used to compare continuous variables while proportions were used to compare categorical variables. Logistic regression was used to determine factors most associated with second line ART treatment. All variables with p value ≤ 0.2 in univariate analysis were included in the multivariate analysis. All variables with a p value ≤ 0.05 were considered significant.

***Ethics consideration***

Ethics clearance with reference number MU/PGS/SAEC/Vol.IX/ was obtained from the Research and Ethics Committee of Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct the study at Amana and Amtulabhai clinics was obtained from Ilala Municipality District Medical Officer's office. All participants gave informed consent for participation.

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**Results**

We recruited 102 patients on first-line and 102 patients on second line HIV treatment. The median (IQR) age at the time of the study for all the 204 patients was 42 (36.3-49) years, being 43(37-49) for Patients on second-line ART and 41.5(35-49) for patients on first-line (not shown in Table 1). Table 1 compares socio-demographic, clinical and laboratory characteristics of patients on first-line and those on second-line treatment. Female participants were the majority constituting 73.5% of patients on first-line and 63.7% of patients on second-line treatment. Ilala and Kinondoni municipality had more of the patients (36.3%) who received second-line treatment at AKC than was Temeke municipality (25.5%). Significantly more patients on second-line ART were employed compared to those on first-line; 90.2% vs 72.4% respectively, p=0.001, had been on ART for 60 or more months, 71.6% vs 33.3% respectively, p<0.001, had changed their ART regimen three times or more compared to those on first-line ART, 16.7% vs 3.9% p<0.003. Patients on second-line ART significantly had lower median(IQR) pre-ART CD4 counts compared to those on first-line ART, 72 (26-192) cells/µL vs 150(61-273) cells/ µL respectively, p=0.03, presented with lower median(IQR) current CD4 counts at the time of the study than were patients on first-line ART, 326 (213-412) cells/µL vs 422(299-583) cells/µL respectively, p<0.001. Additionally, patients on second-line ART were found to have higher median (IQR) creatinine level and higher median (IQR) platelet counts (p<0.05) (**Table 1**)

In univariate analysis, having no formal education or primary level education, being employed, having a Pre-ART CD4 cell count of <100cells/µL, using ART >60 months and having changed ART 3 or more times were significantly associated with second-line ART (p<0.05). Female sex was also found to be associated with second-line ART use in univariate analysis (p<0.2). After controlling for the effect of sex, education, number of times ART were changed, and duration of use of ART the odds of being on second line ART were 2.5 times higher among patients who were working compared to those who were not having any form of employment, OR (95%CI) = 2.47 (1.03-5.90), p= 0.042. Patients with a pre-ART CD4 cell ≥100cells/µL had a 44% decreased likelihood of being on second-line ART but this was not significant, OR (95% CI) = 0.56 (0.30-1.04), p=0.064. After controlling for the effect of sex, education, number of times ART were changed, the odds of being on second line ART were 4.3 times higher among patients who were on ART for more than 60 months compared to those who were on ART for 60 months or less. OR (95% CI) = 4.32 (2.30-8.12), p<0.001.

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**Table 1: Socio-demographic and clinical characteristics of patients on first line and second line ART, N=204**

| Parameter | | First Line N=102 Number (%) | Second line N=102 Number (%) | Total N=204 Number (%) | P-*Value* |
|---|---|---|---|---|---|
| **Age at ART initiation (years)** | <40 | 60(58.8) | 66(64.7) | 126(61.8) | |
| | ≥40 | 42(41.2) | 36(35.3) | 78(38.2) | 0.236 |
| **Age at the time of the study (years)** | <40 | 41(40.2) | 37(36.3) | 78(38.2) | |
| | ≥40 | 61(59.8) | 65(63.7) | 126(61.8) | 0.333 |
| **Sex: Female** | | 75(73.5) | 65(63.7) | 140(68.6) | 0.13 |
| **Residence:** | Ilala | 81(79.4) | 37(36.3) | 118(57.8) | <0.001* |
| | Kinondoni | 16(15.7) | 37(36.3) | 53(26) | |
| | Temeke | 5(4.9) | 26(25.5) | 31(15.2) | |
| | Outside Dar es Salaam | 0(0) | 2(2) | 2(1) | |
| **Marital Status:** | Ever married | 67(65.7) | 77(75.5) | 144(70.6) | |
| | Never married | 35(34.3) | 25(24.5) | 60(29.4) | 0.49 |
| **Education:** | None | 6(5.9) | 7(6.9) | 13(6.4) | |
| | Primary | 75(73.5) | 59(57.8) | 134(65.7) | |
| | Secondary/Post - secondary | 21(20.6) | 36(35.3) | 57(28.0) | 0.08 |
| **Occupation:** | Unemployed | 28(27.5) | 10(9.8) | 38(18.6) | |
| | Employed* | 74(72.5) | 92(90.2) | 166(81.4) | 0.001 |
| **Monthly Income (Tsh)** | ≤500,000/= | 90(88.2) | 91(89.2) | 181(88.7) | |
| | >500,000/= | 12(11.8) | 11(10.8) | 23(11.3) | 0.825 |
| **Disclosed their HIV status** | | 98(96.1) | 101(99) | 199(97.5) | 0.17 |

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| | | | | | |
|---|---|---|---|---|---|
| **Duration of ART use:** | ≤60 months | 68(66.7) | 29(28.4) | 97(47.5) | |
| | >60 months | 34(33.3) | 73(71.6) | 107(52.5) | <0.001 |
| **Missing ART doses/month** | ≤2 doses/month | 90(88.2) | 89(87.3) | 179(90.4) | 0.83 |
| | >2 doses/month | 12(11.8) | 13(12.7) | 25(12.3) | |
| **Past TB treatment** | | 10(9.8) | 14(13.7) | 24(11.8) | 0.39 |
| **Number of times ART were changed** | 1-2 regimen | 98(96.1) | 85(83.3) | 183(89.7) | |
| | ≥3 regimen | 4(3.9) | 17(16.7) | 21 (10.3) | 0.003 |
| **Laboratory parameters (Medians, Interquartile range)** | **Pre-ART CD4 count** cells/µL | 150(61-273) | 72(26-192) | 99(39-228) | 0.03 |
| | **CD4 count** at the time of the study (cells/µL) | 422(299-583) | 326(213-412) | 389 (236-509) | <0.001 |
| | Hemoglobin (g/dl), | 12.2 (11.3-13) | 11.8 (10.6-13.3) | 12 (10.9-13) | 0.39 |
| | ALT (units/litre), | 20.1 (15.4-29) | 23 (13.1-39) | 21 (14-33) | 0.10 |
| | Creatinine (mg/dl), | 0.78 (0.66-0.9) | 0.9 (0.75-1.2) | 0.81 (0.69-1.01) | <0.001 |
| | Neutrophils (value x $10^9$/L), | 2.1 (1.7-2.9) | 2.2 (1.5-2.8) | 2.1 (1.6-2.8) | 0.76 |
| | Platelets (value x $10^9$/L), | 217 (171-287) | 240 (179-321) | 224(175-300) | 0.02 |

***Key:*** **Fisher's exact test, ART – antiretroviral therapy; HIV – Human immunodeficiency virus; Tsh – Tanzanian shillings (where at the time of the study 1 US dollar= 2250 Tsh); TB – Tuberculosis, *Employment included, self-employment, government and private employment.*

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**Table 2: Factors associated with second-line ART treatment by logistic regression, N=204**

| Parameter | Unadjusted OR (95% CI) | P-value | Adjusted OR (95% CI) | P value |
|---|---|---|---|---|
| **Age groups at the time of the study (years)*** | | | | |
| <40 | 1 | | | |
| ≥40 | 0.85(0.48-1.49) | 0.565 | | |
| **Age at ART initiation (years)*** | | | | |
| <40 | 1 | | | |
| ≥40 | 0.79 (0.45-1.41) | 0.437 | | |
| **Sex:** | | | | |
| Male | 1 | | 1 | |
| Female | 1.6(0.87-2.87) | 0.133 | 1.1(0.55-2.1) | 0.800 |
| **Marital status*** | | | | |
| Ever married | 1 | | | |
| Never married | 0.96 (0.56-1.67) | 0.889 | | |
| **Education** | | | | |
| None or primary level | 1 | | 1 | |
| Secondary level or higher | 0.48 (0.25-0.89) | 0.020 | 0.51 (0.25-1.03) | 0.061 |
| **Occupation** | | | | |
| Unemployed | 1 | | 1 | |
| Employed | 3.48 (1.59-7.62) | 0.002 | 2.47 (1.03-5.90) | 0.042 |
| **HIV status disclosure to specific people*** | | | | |
| Yes | 1 | | | |
| No | 4.12(0.45-37.54) | 0.209 | | |
| **Monthly income*** | | | | |
| ≤500,000 Tsh | 1 | | | |
| >500,000 Tsh | 1.10 (0.46-2.63) | 0.825 | | |
| **Pre-ART CD4 cell count** | | | | |
| <100 cells | 1 | | 1 | |
| ≥100 cells | 0.51 (0.29-0.89) | 0.018 | 0.56 (0.30-1.04) | 0.064 |
| **Duration of ART use** | | | | |
| ≤60 months | 1 | | 1 | |
| > 60 months | 5.03 (2.78-9.13) | <0.001 | 4.32 (2.30-8.12) | <0.001 |
| **Number of ART regimen ever used** | | | | |
| 1-2 | 1 | | 1 | |
| ≥3 | 0.20 (0.07-0.63) | 0.006 | 0.44 (0.13-1.50) | 0.181 |
| **Missed ART doses/month*** | | | | |
| ≤2 doses | 1 | | | |
| > 2 doses | 1 | 1.000 | | |

***Not part of the multivariate analysis (p>0.2)*

*Key: ART – antiretroviral therapy; HIV – Human immunodeficiency virus; Tsh – Tanzanian shillings (where at the time of the study 1 US dollar= 2250 Tsh);*

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**Discussion**

We have presented characteristics of patients on second-line antiretroviral drugs in Dar es Salaam, Tanzania. Patients on second line ART significantly presented with the following characteristics: employment, longer duration on ART, multiple changes of ART regimen, lower levels of CD4 counts in pre-ART and at the time of the study, high median serum creatinine and median platelets. Pre-ART CD4 counts < 100 cells/µL and having no education or primary level education had borderline significance.

More than three thirds of the patients on second-line ART at AKC had used ART for more than 60 months. Although it was not possible to clearly establish the exact duration of use of the first line ART for every patient in second line ART, it was obvious that those on first line ART had used ART for shorter durations than those in the second line ART. Studies have demonstrated that longer duration of ART is associated with antiretroviral drug resistance(22,23), probably through sub-optimal adherence and thus emergence of mutations. We are inferring that probably patients on second line ART in the present study had used ART for many years before switching to second line, given their comparability of current age to those in the first line ART. The longer duration on ART increases the chance of missing medications and thus more susceptibility to drug resistance.

In the present study we found that there were more employed participants on the second-line ART group than were on first-line ART group. Employment remained a significant predictor of being on second line ART even after controlling for possible confounders in logistic regression. Our definition of employment included employment by the government, private sector and self. In the present study self-employment constituted 71% of the employed people in the second-line ART. In Tanzania, most of self-employed people do petty trades. Speculations can be made that adherence might be at stake if one feels that attending a clinic for almost a whole day would compromise a business. The finding in the present study call upon further investigations of the various self-employments to see if they do confer better social support, better structuring of time and improved psychosocial well-being. A meta-analysis by Nachega *et al* had linked unemployment with ART resistance through poor adherence which was seen more on unemployed people compared to employed ones(24). Employment definition in the meta-analysis was unclear.

Significantly more patients on second-line ART had pre-ART CD4 counts below 100 cells/µl, compared to patients on first-line ART. Although Pre-ART CD4 counts in the present study had boarderline significant relationship with second-line ART, Low pre-ART CD4 counts have been

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reported to be significant predictor of ART treatment failure in other studies (25–27). Explicitly, patients with CD4 counts below 100 cells/µl are more likely to be very sick and on treatment for various opportunistic infections including those causing diarrhea, malabsorption and vomiting. ART drug interactions with drugs causing cytochrome P450 enzyme induction like Rifampicin are also a possibility in this scenario. All these might in a way interfere with the bioavailability of the ART.

The potential limitation of the present study is its observational nature hence failure to establish cause and effect. There is also a possibility that patients in the two study sites were quite different although some of those on second line ART originated from Amana clinic. Duration of treatment before treatment failure could inform better the situation among patients on second line ART than the overall treatment duration used in the current study. Furthermore, we wished we could obtain enough viral load counts and check the relationship of opportunistic infections other than TB with treatment failure. We recommend prospective studies to assess adherence to ART and other characteristics that we couldn't assess in HIV infected patients on second line at the pre-treatment failure time.

**Conclusion**

Patients on second line ART at AKC had commenced their 1st line ART with severe immunosuppression, had changed their ART regimen thrice or more, had lower CD4 counts at the time of the study and had been generally on ART for more than five years contrary to patients on first-line ART. Having an employment and being on ART for more than 60 months was associated with being on second-line ART in the study population. We recommend more efforts on advocating active screening for HIV and early ART treatment before severe depression of the immune system.

**Authors' contribution**

GAS, FBS and FMM designed the study. GAS and FBS supervised data collection. FBS entered data into the computer. GAS, FBS and SFM analyzed the data. GAS wrote the first manuscript draft. All read, improved and approved the final manuscript for publication.

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nurses and laboratory technicians at AKC and Amana hospital. Appreciation is sent to Prof. Rose Mpembeni and Dr. Candida Moshiro of Muhimbili University of Health and Allied Sciences for their advice on statistics.

**Abbreviations**

| | |
|---|---|
| AIDS | Acquired Immunodeficiency Syndrome |
| 3TC | Lamivudine |
| ABC | Abacavir |
| AKC | Amtulabhai Karimjee Clinic |
| ART | Antiretroviral Therapy |
| ATV/r | Atazanavir boosted by Ritonavir |
| AZT | Zidovudine |
| CD4 | Cluster of Differentiation 4 |
| CNS | Central Nervous Syatem |
| CTC | Care and Treatment Centre |
| d4T | Stavudine |
| EDTA | Ethylenediaminetetraacetic acid |
| EFZ | Efavirenz |
| FTC | Emtricitabine |
| HIV | Human Immunodeficeiency virus |
| ICOHRTA | International Clinical, Operational and Health Services Research and Training Award |
| IQR | Interquartile range |
| LPV/r | Lopinavir boosted by Ritonavir |
| MUHAS | Muhimbili University of Health and Allied Sciences |
| NIH | National Institutes of Health |
| NNRTIs | Non-Nucleoside Analogue Reverse Transcriptase Inhibitors |
| NRTIs | Nucleoside Analogue Reverse Transcriptase Inhibitors |
| NVP | Nevirapine |
| PEPFAR | President's Emergency Plan for AIDS Relief |
| PIs | Protease inhibitors |
| TB | Tuberculosis |
| U.S.A | United States of America |
| VL | Viral load |
| WHO | World Health Organization |

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**References**

1. **WHO. Report on the global AIDS epidemic** [Internet]. Vol. 2010. 2009. Available from: http://www.unaids.org/sites/default/files/media_asset/jc1510_2008globalreport_en_0.pdf
2. Trickey A, May MT, Vehreschild J-J, Obel N, Gill MJ, Crane HM, et al. **Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies.** Lancet HIV [Internet]. 2017;4(8):e349–56. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2352301817300668
3. Crummy F, Piper AJ, Naughton MT. **Obesity and the lung: 2. Obesity and sleep-disordered breathing.** Thorax [Internet]. 2008 Aug [cited 2014 Jun 4];63(8):738–46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18663071
4. Palella F, Delaney K, Moorman A, Loveless M, Fuhrer J, Satten G, et al. **Declining Morbidity and Mortality among Patients with Advance Human Immunodeficiency Virus Infection.** N Engl J Med. 1998;338(13):853–60.
5. Crum NF, Riffenburgh RH, Wegner S, Agan BK, Tasker S a, Spooner KM, et al. **Comparisons of Causes of Death and Mortality Rates Among HIV-infected persons. Analysis of the pre-, Early, and Late HAART(Highly Active Retroviral Therapy)** Eras. J Acquir Immune Defic Syndr. 2006;41(2):194–200.
6. **The Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies**. Lancet HIV. 2017;4(8):e349–56.
7. Johnson LF, Mossong J, Dorrington RE, Schomaker M, Hoffmann CJ, Keiser O, et al. **Life Expectancies of South African Adults Starting Antiretroviral Treatment: Collaborative Analysis of Cohort Studies.** PLoS Med. 2013;10(4).
8. Kaiser Family Foundation based on WGTR 2014. **TB high burden countries**.pdf [Internet]. 2014. Available from: http://kff.org/globaldata/
9. Candiani T, Pinto J, Cardoso C, Carvalho I, Dias a, Carneiro M, et al. **Impact of highly active antiretroviral therapy ( HAART ) on the incidence of opportunistic infections , hospitalizations and mortality among children and adolescents living with HIV / AIDS in Belo Horizonte , Minas Gerais State , Brazil Impacto da terapia. Cad Saude Publica** [Internet]. 2007;23(3):414–23. Available from: http://www.scielo.br/pdf/csp/v23s3/09.pdf
10. Engels EA, Pfeiffer RM, Goedert JJ, Virgo P, McNeel TS, Scoppa SM, et al. **Trends in cancer risk among people with AIDS in the United States 1980-2002**. AIDS. 2006;20(12):1645–54.
11. Patel P, Hanson DL, Sullivan PS, Novak RM, Moorman AC. **Incidence of Types of Cancer**

**among HIV-Infected Persons Compared with the General Population in the United States , 1992 – 2003.** Ann Intern Med [Internet]. 2008;(Cdc):1992–2003. Available from: http://www.annals.org/content/148/10/728.long

12. Hellinger F. **The changing pattern of hospital care for persons living with HIV : 2000 through 2004 .** J Acquir Immune Defic Syndr. 2007;45(2):239–46.
13. Vella S, Palmisano L. **The global status of resistance to antiretroviral drugs.** Clin Infect Dis [Internet]. 2005;41 Suppl 4(Supplement 4):S239-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16032559
14. Xing H, Ruan Y, Li J, Shang H, Zhong P, Wang X, et al. **HIV Drug Resistance and Its Impact on Antiretroviral Therapy in Chinese HIV-Infected Patients.** PLoS One. 2013;8(2):1–7.
15. Hawkins C, Ulenga N, Liu E, Aboud S, Mugusi F, Chalamilla G, et al. **HIV virological failure and drug resistance in a cohort of Tanzanian HIV-infected adults**. J Antimicrob Chemother. 2016;71(7).
16. Hawkins C, Ulenga N, Liu E, Aboud S, Mugusi F, Chalamilla G, et al. **HIV virological failure and drug resistance in a cohort of Tanzanian HIV-infected adults.** J Antimicrob Chemother. 2016;71(7):1966–74.
17. Xing H, Wang X, Liao L, Ma Y, Su B, Fu J, et al. **Incidence and Associated Factors of HIV Drug Resistance in Chinese HIV-Infected Patients Receiving Antiretroviral Treatment.** PLoS One. 2013;8(4):4–9.
18. Bezabih YM, Beyene F, Bezabhe WM. **Factors associated with first-line antiretroviral treatment failure in adult HIV-positive patients: A case-control study from Ethiopia.** BMC Infect Dis. 2019;19(1):1–8.
19. **World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection**. Recommendations for a Public Health Approach [Internet]. Geneva, Switzerland; 2016. Available from: https://www.who.int/hiv/pub/arv/arv-2016/en/
20. Johannessen A, Naman E, Kivuyo SL, Kasubi MJ, Holberg-Petersen M, Matee MI, et al. **Virological efficacy and emergence of drug resistance in adults on antiretroviral treatment in rural Tanzania.** BMC Infect Dis. 2009;9:108.
21. Muri L, Gamell A, Ntamatungiro AJ, Glass TR, Luwanda LB, Battegay M, et al. Development of HIV drug resistance and therapeutic failure in children and adolescents in rural Tanzania: An emerging public health concern. AIDS. 2017;31(1):61–70.
22. Jiamsakul A, Sungkanuparph S, Law M, Kantor R, Praparattanapan J, Li PCK, et al. **HIV**

**multi-drug resistance at first-line antiretroviral failure and subsequent virological response in Asia.** J Int AIDS Soc. 2014;17:1–10.

23. Fofana DB, Soulié C, Baldeé A, Lambert-Niclot S, Sylla M, Ait-Arkoub Z, et al. **High level of HIV-1 resistance in patients failing long-term first-line antiretroviral therapy in Mali.** J Antimicrob Chemother. 2014;69(9):2531–5.
24. Nachega JB, Uthman OA, Peltzer K, Richardson LA, Mills EJ, Amekudzi K, et al. **Association between antiretroviral therapy adherence and employment status: systematic review and meta-analysis.** Bull World Health Organ [Internet]. 2015;93(1):29–41. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4271680&tool=pmcentrez&rendertype=abstract
25. Khienprasit N, Chaiwarith R, Sirisanthana T, Supparatpinyo K. **Incidence and risk factors of antiretroviral treatment failure in treatment-naïve HIV-infected patients at Chiang Mai University Hospital, Thailand.** AIDS Res Ther [Internet]. 2011;8(1):42. Available from: http://www.aidsrestherapy.com/content/8/1/42
26. Kwobah CM, Mwangi AW, Koech JK, Simiyu GN, Siika AM. **Factors Associated with First-Line Antiretroviral Therapy Failure amongst HIV-Infected African Patients: A Case-Control Study.** World J AIDS. 2012;2(July 2011):271–8.
27. Robbins GK, Daniels B, Zheng H, Chuen H, Meigs JB, Freedberg KA. **Predictors of Antiretroviral Treatment Failure in an Urban Clinic.** J Acquir Immune Defic Syndr. 2007;44(1):30–7.