

# Detection of Antiretroviral treatment failure among adult HIV-1 patients on anti-retroviral therapy for 12 +/- 3 months attending different Voluntary Counseling Testing and treatment centers in Khartoum state, Sudan

Nafisa Ahmed Ibrahim (✉ [nafosa88@gmail.com](mailto:nafosa88@gmail.com))

Neelain University Faculty of Medical Laboratory Sciences <https://orcid.org/0000-0002-7146-799X>

Khalid A Enan

Department of Virology\_ Central laboratory\_ Sudan

Mahdi Mustafa Yagoup

Senior HIV clinical Mentor/ Case management Unit DCD\_ Fedral Ministry of Health, Sudan

Wafa Ibrahim Elhag

Collage of Medicine\_ University of Bisha (Saudi Arabia)\_ Faculty of Medical Laboratory Sciences, Al Neelain University, Sudan

---

## Research note

**Keywords:** Sudan, HIV-1 viral load, Gene Xpert, ART treatment failure

**Posted Date:** October 27th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-96321/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Objective:** Small number of people on antiretroviral therapy and their virological status in Sudan is lacking. This study aimed to determine the viral load for adult HIV-1 patients who were on antiretroviral therapy for 12+/- 3 months attending different Voluntary Counseling Testing and treatment centers (VCT/ART) in Khartoum state, Sudan.

**Results:** out of 112 adult HIV-1 patients included in this study, only 17.9% (20/112) showed unsuppressed viral load (treatment failure). The majority of them from Omdurman VCT/ART center 80% (16/20), followed by Khartoum VCT/ART center 15% (3/20), Bahri VCT/ART center 5% (1/20) and non from Elban Gadeid VCT/ART center. All of them were on the first line of treatment. Most of them 30% (6/20) on 39-48 years old age group, the majority of them 55%(11/20) on stage 3 WHO clinical staging.

## Introduction

More than 14.5 of the 36.7 million individuals living with HIV all over the world don't have the clear idea about their HIV status, so making exhaustive testing intervention a basic step in closure the HIV/AIDS epidemic <sup>(1)</sup>.

Sudan is one of the areas that enclosed by countries with higher rate of HIV infection. The prevalence was 1.6% in 2002 <sup>(2)</sup>. As indicated by UNAIDS 2011, the prevalence was diminished to 0.4% after South Sudan dissociation. In 2018 it was diminished to 0.2%.<sup>(3)</sup>

In Sudan, 2018, adults living with HIV were 55000, among them, only 9000 (15%) were on antiretroviral therapy (ART) and no data about people living with HIV who have suppressed viral loads <sup>(3)</sup>

In areas with satisfactory resources, research center estimations of CD4 + T cells and plasma HIV viral load are usually used to build up a patient's level of immunosuppression and the rate of destruction of the immune system, these are used to ascertain a patient's eligibility for treatment and also monitor disease progression <sup>(4)</sup>. In resource limited areas in which deficient settings to test CD4 + T cells and plasma HIV viral load, clinicians depend on the clinical parameters while assessing a patient's disease status.

HIV-1 viral load testing is an essential part of HIV-1 management in the world, both before and during antiretroviral therapy <sup>(5)</sup>. The amount of virus present in the plasma affects clinical decisions; therefore, accurate sensitive viral load assays are very important.

Monitoring HIV viral load in people living with HIV is essential to maintain effective individual antiretroviral therapy as well as monitoring progress toward achieving population targets for viral suppression<sup>(6)</sup>. It is an excellent predictor of survival to AIDS and death<sup>(7, 8)</sup> with a better correlation and independent of CD4 count<sup>(9, 10)</sup>.

Viral loads exceeding 50 copies/ml always need further investigations, and > 1,000 copies/ml (> 3 log copies/ml) is considered to be the threshold for resistance testing<sup>(11, 12)</sup> and in this case, the WHO recommends a confirmatory viral load measurement 3 months after the first viral load and enhanced adherence support, with switch to second-line ART contingent upon a continued elevated viral load<sup>(13)</sup>. Without drug resistance, HIV-positive patients should achieve viral suppression within 8–24 weeks after ART initiation<sup>(14, 15)</sup>

In 2014 the Joint United Nations Program on HIV and AIDS (UNAIDS) set a determined target known as the 90-90-90, that indicated that by 2020, 1) 90% of all HIV positive people will be diagnosed, 2) 90% of all those diagnosed will be on treatment and 3) 90% of those linked to care will be virally suppressed.<sup>(16)</sup>

So this study aimed to estimate the viral load for adult HIV-1 patients who were on antiretroviral therapy for 12 +/- 3 months attending different Voluntary Counseling Testing and treatment centers (VCT/ART) in Khartoum state, Sudan.

## Methods

### Study population, area and duration

The study was descriptive cross sectional health facility based. It was conducted in 112 adult ( $\geq$  18 years) HIV-1 patients attending four VCT/ART clinics centers distributed in Khartoum state, Sudan, including Omdurman Teaching Hospital, Khartoum Teaching Hospital, Bahri Teaching Hospital and Elban Gadeid Hospital from February 2019 to February 2020. All randomly selected HIV-1 patients were on ART for 12 +/- 3 months

All participants were provided with written informed consent for guarantees of approval and confidentiality and then data (age, sex, WHO clinical stage and ART type and initiation date) were collected from patient management records from VCT/ART centers.

### Blood samples collection, HIV-1 detection and quantification

Six ml of blood samples were collected in Ethylene diamine tetraacetic acid (EDTA) blood collection tubes. Plasma were separated by centrifugation at 5000 rpm for 5 minutes and stored in multiple aliquots at -80° C until used

On the day of analysis, the aliquots were thawed, vortex-mixed, and tested for antibodies detection specific to HIV-1 using 4th generation ELISA kit (Fortress diagnostics, United Kingdom) according to manufacturer instructions.

The remaining plasma (one ml) were taken for HIV-1 RNA viral load quantification by multiplex real time PCR, Cepheid Xpert HIV-1 viral load plasma assay (Cepheid, Inc., Sunnyvale, CA), according to manufacturer instructions, which had sensitivity above 95% in treatment failure detection<sup>(17)</sup>

## Data Analysis

Data were analyzed by SPSS program version 23, using frequencies and cross tab

## Results

Of the 112 patients that met the inclusion criteria, the majority of the patients belong to Omdurman VCT/ART center 60.7% (68/112), followed by Khartoum teaching hospital VCT/ART center 17.9% (20/112), Bahri teaching hospital VCT/ART center 16.1% (18/112) and Elban Gadeid VCT/ART center 5.4% (6/112).

The age ranged from 19–70 years old with 44.5 years mean (Fig. 1), 58% (65/112) were males, 42% (47/112) were females. 95.5% (107/112) were in the first line of ART and 4.5% (5/112) on the second line. The majority of the patients were on stage 3 according to WHO clinical staging 54.5% (61/112), followed by stage 1, stage 2 and stage 4 by frequencies 23.5% (26/112), 18.8% (21/112) and 3.6% (4/112) respectively.

The viral load results ranged from none detected copies/ml to more than 1000 copies/ml. The majority of the patients have suppressed viral load results, non detected copies/ml, 37.5% (42/112) followed by 35.7% (40/112) less than 40 copies/ml, 17.9% (20/112) more than 1000 copies/ml, 7.1% (8/112) less than 1000 copies/ml and 1.8% (2/112) had invalid results. (Fig. 2)

Out of 17.9% (20/112) patients with unsuppressed viral load, the majority 80% (16/20) belonged to Omdurman VCT/ART center followed by Khartoum VCT/ART center 15% (3/20), Bahri VCT/ART center 5% (1/20) and Elban Gadeid VCT/ART center 0% (0/20).

All patients with unsuppressed viral load were on the first line of treatment. Most of them 30% (6/20) on 39–48 years old age group and the majority of them 55% (11/20) on stage 3 regarding WHO clinical staging

## Discussion

Viral load is the preferred treatment-monitoring approach for HIV-positive patients. In Sudan, Gene Xpert was approved by WHO and introduced as a tool for TB/ HIV-1 diagnosis and monitoring respectively. It is rapid and less complexity assay<sup>(18)</sup>

The present study result was similar to many studies results that showed low number of unsuppressed viral load patients. As in study conducted in South Africa in 2018, the percentage of patients in the first line of treatment with virological failure was 22%<sup>(19)</sup>. Also studies done in Ethiopia in 2019<sup>(20)</sup> and Uganda in 2015<sup>(21)</sup> the percentage was 11% although their HIV frequency is higher than Sudan.

Regarding sex status, the number of males were higher than females (58% versus 42%) in this study, which is similar to study done in Sudan in 2015 in which males were higher<sup>(22)</sup>, however it was dissimilar

to the study done in Ethiopia in 2019 in which the females were higher in number<sup>(20)</sup>.

The most higher WHO clinical stage of HIV was stage 3 in this study, which is dissimilar to study done in India in 2019 in which the most common unsuppressed patients were in stage 1<sup>(23)</sup>

The virological failure was observed in the age group 39–48 years, which is similar to the finding of the study done in Ethiopia in which virological failure was observed among patients aged < 35 years<sup>(20)</sup>

Most of patients 82.1% had suppressed viral load (non detectable copies/ ml and less than 40 copies/ ml) because viral load usually become not detected after  $12 \pm 3$  month successful treatment, while patients with unsuppressed viral load may need a good adherence, they may have metabolic problems or they may have drug resistance mutations. This finding put Sudan closer to the UNAIDS treatment target 2020 in which 90% of patients under treatment must have suppressed viral load.

## Conclusion

Establishment of a good ART program, routine and regular patients follow up and improving adherence can decrease the virological failure and improve treatment outcome.

### Limitations

The present study was the first study done in Sudan, it does not cover all the patients on ART for 12 months +/- 3 months attending ART/VCT centers. Also it covers only four centers out of eight centers in Khartoum state, Sudan, so the results does not reflect and represent the whole HIV-1 patients in the country.

## List Of Abbreviations

HIV-1: Human Immunodeficiency Virus -1; VCT centers: Voluntary Counseling Testing and treatment centers; ART: Antiretroviral therapy; AIDS: Acquired Immunodeficiency Syndrome; WHO: World Health Organization; UNAIDS: United Nation Acquired Immunodeficiency Syndrome program; RNA: Ribonucleic Acid; EDTA: Ethylene diamine tetraacetic acid

## Declarations

### Ethics approval and consent to participate

The study was approved by the Institutional Review Board of Al Neelain University, Deanship of Scientific Research, Sudan.

All participants were provided with written informed consent for guarantees of approval and confidentiality (Additional file 1).

Not applicable

### **Availability of data and materials**

All dataset used and analyzed at this study is found within an additional Microsoft Word document file (Additional file 2)

### **Competing interests**

All authors declare that they have no competing interest

### **Funding**

Not applicable

### **Authors' contributions**

All authors read and approved this final manuscript. NAI made the collection and laboratory work of the samples, also drafted and designed the paper for publication and analyzes the results. KAE revised the manuscript and supervise the laboratory work. MMY facilitates the samples availability and revised the manuscript. WIE supervised all the experimental work, review and corrects the manuscript

### **Acknowledgments**

Our thanks and regards to WHO Sudan and National Central laboratory for their support, guidance and helping to achieve this work. Also deep thanks to all included VCT/ART center, Khartoum, Sudan, in this research for their co-operation.

## **References**

1. Hauck K. The costs of home-based HIV testing and counselling in sub-Saharan Africa and its association with testing yield: a literature review. *African Journal of AIDS Research*. 2019;18(4):324-31.
2. Mohamed BA, Mahfouz MS. Factors associated with HIV/AIDS in Sudan. *BioMed research international*. 2013;2013.
3. UNAIDS. Sudan | UNAIDS [cited 2020 15 March]. Available from: [www.unaids.org](http://www.unaids.org) › regionscountries › countries › sudan.
4. Simon V, Ho DD, Karim QA. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. *The Lancet*. 2006;368(9534):489-504.
5. Thompson MA, Aberg JA, Hoy JF, Telenti A, Benson C, Cahn P, et al. Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society–USA panel. *Jama*. 2012;308(4):387-402.

6. Drain PK, Dorward J, Bender A, Lillis L, Marinucci F, Sacks J, et al. Point-of-care HIV viral load testing: an essential tool for a sustainable global HIV/AIDS response. *Clinical microbiology reviews*. 2019;32(3):e00097-18.
7. Ho DD, Moudgil T, Alam M. Quantitation of human immunodeficiency virus type 1 in the blood of infected persons. *New England journal of medicine*. 1989;321(24):1621-5.
8. Riddler S, Mellors J. HIV-1 viral load and clinical outcome: review of recent studies. *AIDS (London, England)*. 1997;11:S141.
9. Mellors JW, Kingsley LA, Rinaldo CR, Todd JA, Hoo BS, Kokka RP, et al. Quantitation of HIV-1 RNA in plasma predicts outcome after seroconversion. *Annals of internal medicine*. 1995;122(8):573-9.
10. O'Brien TR, Blattner WA, Waters D, Eyster ME, Hilgartner MW, Cohen AR, et al. Serum HIV-1 RNA levels and time to development of AIDS in the Multicenter Hemophilia Cohort Study. *Jama*. 1996;276(2):105-10.
11. Organization WH. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach: World Health Organization; 2016.
12. Doyle T, Smith C, Vitiello P, Cambiano V, Johnson M, Owen A, et al. Plasma HIV-1 RNA detection below 50 copies/ml and risk of virologic rebound in patients receiving highly active antiretroviral therapy. *Clinical Infectious Diseases*. 2012;54(5):724-32.
13. Shroufi A, Van Cutsem G, Cambiano V, Bansi-Matharu L, Duncan K, Murphy RA, et al. Simplifying switch to second-line antiretroviral therapy in sub Saharan Africa: predicted effect of using a single viral load to define efavirenz-based first-line failure. *AIDS (London, England)*. 2019;33(10):1635.
14. Stevens WS, Marshall TM. Challenges in implementing HIV load testing in South Africa. *Journal of Infectious Diseases*. 2010;201(Supplement\_1):S78-S84.
15. McMahon JH, Elliott JH, Bertagnolio S, Kubiak R, Jordan MR. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review. *Bulletin of the World Health Organization*. 2013;91:377-85.
16. Global H. AIDS statistics—2018 fact sheet. UNAIDS website [unaids.org/en/resources/fact-sheet](http://unaids.org/en/resources/fact-sheet) Accessed May. 2019;31.
17. Sacks JA, Fong Y, Gonzalez MP, Andreotti M, Baliga S, Garrett N, et al. Performance of Cepheid Xpert HIV-1 viral load plasma assay to accurately detect treatment failure. *Aids*. 2019;33(12):1881-9.
18. Nash M, Huddart S, Badar S, Baliga S, Saravu K, Pai M. Performance of the Xpert HIV-1 viral load assay: a systematic review and meta-analysis. *Journal of clinical microbiology*. 2018;56(4).
19. Hermans LE, Moorhouse M, Carmona S, Grobbee DE, Hofstra LM, Richman DD, et al. Effect of HIV-1 low-level viraemia during antiretroviral therapy on treatment outcomes in WHO-guided South African treatment programmes: a multicentre cohort study. *The Lancet Infectious diseases*. 2018;18(2):188-97.
20. Getaneh Y, Egziabhier AG, Zealiyas K, Tilahun R, Girma M, Michael GG, et al. Treatment Failure Loading [MathJax]/jax/output/CommonHTML/fonts/TeX/fontdata.js erapy in Ethiopia. *BioRxiv*. 2019:577049.

21. Bulage L, Ssewanyana I, Nankabirwa V, Nsubuga F, Kihembo C, Pande G, et al. Factors associated with virological non-suppression among HIV-positive patients on antiretroviral therapy in Uganda, August 2014–July 2015. BMC infectious diseases. 2017;17(1):326.
22. Osman SM, Osman MM, Osman MM, Magzoub M, Ali SEE. Clinical Presentations of HIV/AIDS Among Sudanese Patients in Khartoum, Sudan. Cough. 2017;14:14.0.
23. Meena B, Meena O. THE CLINICAL STUDY OF PRIMARY DRUG RESISTANCE IN HIV POSITIVE PATIENTS. International Journal of Scientific Research. 2019;8(9).

## Figures

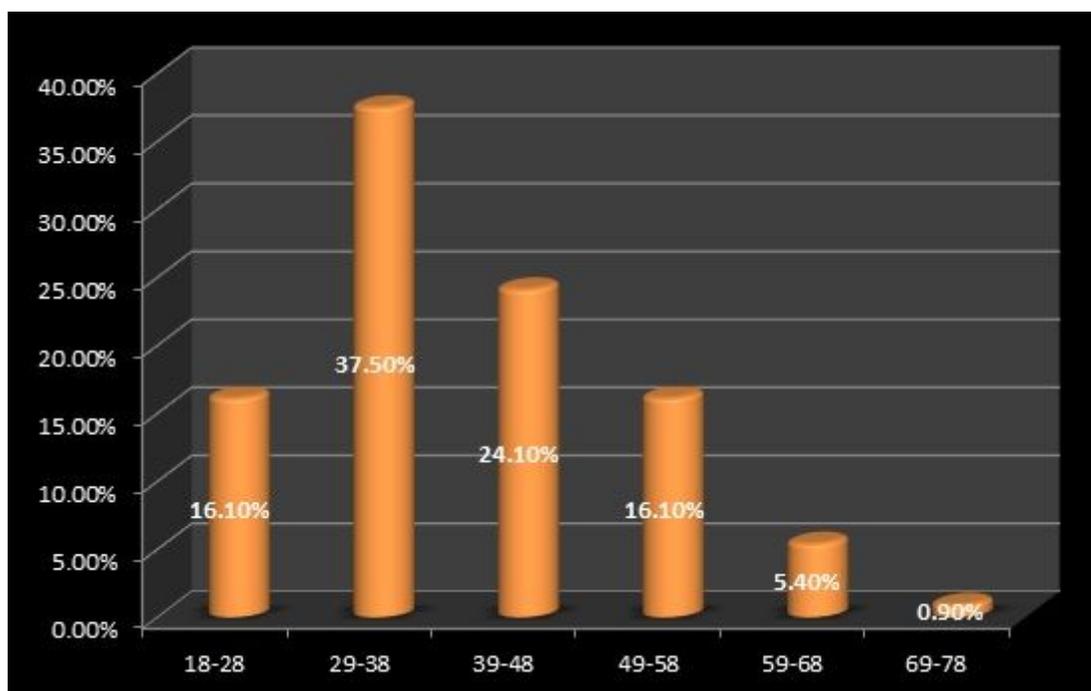
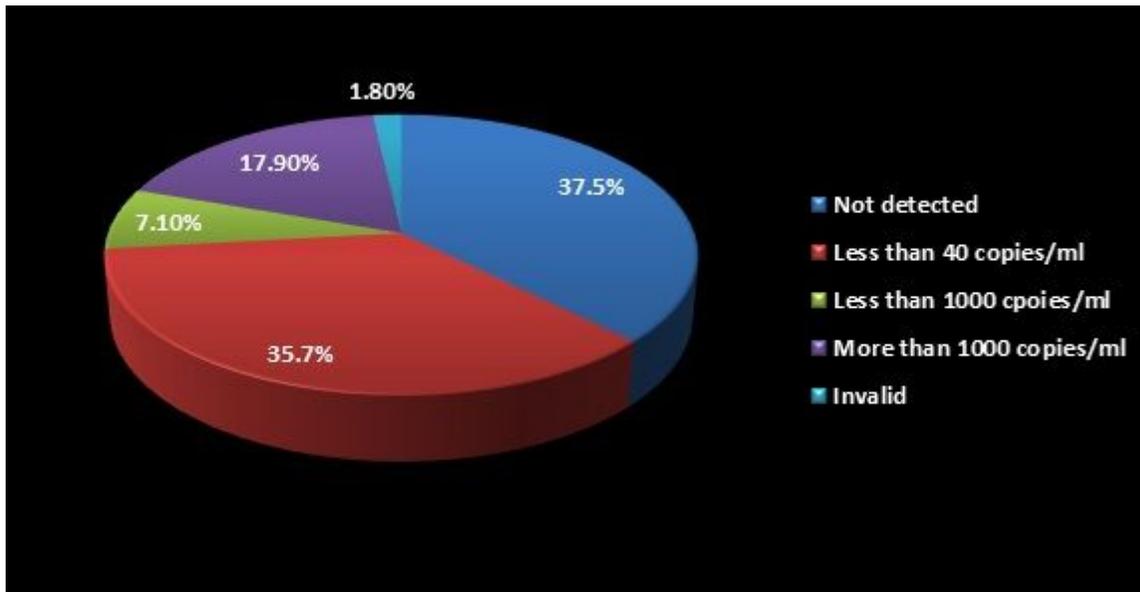


Figure 1

Age range of HIV-1 patients (n=112) on ART 12±3 months attending VCT/ART centers, Khartoum, Sudan



**Figure 2**

HIV-1 viral load results of patients (n=112) on ART 12±3 months attending VCT/ART units, Khartoum-Sudan

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1informedconcent.docx](#)
- [Additionalfile2patientsdatasetandVLresults.docx](#)