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Detection of Antiretroviral Treatment Failure among Adult HIV-1 patients in Khartoum state, Sudan

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Abstract

Background: In 2018, Sudanese adults living with Human Immunodeficiency Virus -1were 55000, among them, only 9000 (15%) were on antiretroviral therapy but no data is available regarding the number of patients living with HIV who have been able to suppress viral loads. **Objectives**: This study aimed to detect antiretroviral treatment failure in adult patients with Human Immunodeficiency Virus-1 (HIV-1) on anti-retroviral therapy for 12±3 months in Khartoum state, Sudan. **Methods**: A hundred and ten adult HIV-1 patients attending four Voluntary Counseling Testing and treatment centers (VCT/ART) distributed in Khartoum state, Sudan were included in this study from February 2019 to February 2020. Patient data were collected from management records and blood samples were collected from them. The HIV-1 viral load was assessed using real-time PCR (Cepheid Xpert HIV-1 viral load plasma assay). **Results**: Out of 110 HIV-1 patients enrolled, only 18.2% (20/110) showed unsuppressed viral load (treatment failure). The majority of patients [30% (6/20)] were from the 39-48 years old age group, and most of them [55% (11/20)]were stage 3 according to WHO clinical staging. The male-female ratio was equal. **Conclusion**: Although the sample size of this study does not represent the whole population, it highlights the presence of treatment failure among HIV-1 patients in Sudan. The establishment of a good treatment program and routine and regular patient follow-up can decrease viral load suppression failure and improve treatment outcomes.

Key words: Sudan; HIV-1; Treatment failure; viral load

Introduction

More than half of the patients living with Human Immunodeficiency Virus (HIV) all over the world do not have a clear idea about their HIV status, so making exhaustive testing interventions is a basic step to putting an end to the global HIV/AIDS epidemic (Hauck, 2019).

Over 20 million people living with HIV/Acquired Immune Deficiency Syndrome (AIDS) are estimated to exist in Africa, and 730,000 new HIV-1 infections still occur every year due to low access to testing (Giovanetti et al., 2020)

Sudan is one of the areas that is surrounded by countries with high rates of HIV infection. The average prevalence of HIV in these countries was 1.6% in 2002 (Mohamed and Mahfouz, 2013). As indicated by United Nations Program on HIV and AIDS(UNAIDS) in 2011, the prevalence in Sudan was diminished to 0.4% after the South Sudan dissociation and in 2018 it diminished to 0.2%. (Sudan, 2020)

In Sudan, in 2018, the adults living with HIV were 55000, among them, only 9000 (15%) were on antiretroviral therapy (ART). No data were available on

the number of patients living with HIV who have successfully suppressed viral loads (Sudan, 2020)

In areas with satisfactory resources, research center estimations of CD4+ T-helper cells and plasma HIV viral loads are usually used to assess a patient's level of immunosuppression and the destruction rate of the immune system. These parameters are used to verify patient eligibility for treatment as well as monitoring of their disease progression (Simon et al., 2006). In resource-limited areas in which low settings test CD4+ T cells and plasma HIV viral load, clinicians depend on the clinical parameters while assessing a patient's disease status.

The amount of virus present in the plasma affects clinical decisions; therefore, HIV-1 viral load testing both before and during antiretroviral therapy is a mainstay of HIV-1 management worldwide (Thompson et al., 2012). Continuous monitoring of 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 (Drain et al., 2019). It is also an outstanding predictor of survival to AIDS and death (Ho et al., 1989, Riddler and Mellors, 1997)) with a better correlation and independent of CD4 count (Mellors et al., 1995, O'Brien et al., 1996).

Antiretroviral therapy (ART) is a type of medication used to treat HIV. These drugs do not kill the virus, but they can prevent it from growing, which has resulted in a dramatic decrease in morbidity and mortality (Rodger et al., 2013).

First-line of ART consisted of 2 nucleosides reverse transcriptase inhibitors, NRTIs mostly zidovudine (AZT) or tenofovir (TDF) and lamivudine (3TC) or emtricitabine (FTC), and 1 non-nucleoside reverse transcriptase inhibitor, NNRTI mostly nevirapine (NVP) or efavirenz (EFV)] as stipulated in the world health organization (WHO) guidelines. (WHo and Unicef, 2011)

Viral loads exceeding 50 copies/ml always need further investigations, and >1,000 copies/ml is the threshold value for resistance testing (Organization, 2016, Doyle et al., 2012) in such cases, the WHO recommends a confirmatory viral load measurement 3 months after the first viral load and intensify adherence support, with the switch to second-line ART if viral load continues to be elevated (Shroufi et al., 2019). In the absence of drug resistance, HIV patients can achieve viral suppression within 8–24 weeks post-ART initiation (Stevens and Marshall, 2010, McMahon et al., 2013)

In 2010 WHO defines three types of criteria to define antiretroviral treatment failure namely, clinical, immunological, and virological failure (Organization, 2013)

In 2014 the Joint UNAIDS set a firm target known as the 90-90-90, which indicated that by 2020, 90% of all HIV-positive people will be diagnosed, 90% of all those diagnosed will be on treatment and 90% of those linked to care will be virally suppressed. (Levi et al., 2016)

Towards the end of 2016, Sudan adopted the WHO treat-all policy. The implementation of the new guidelines has contributed to the improvement of treatment coverage by decreasing losses that used to occur during the pre-ART period. However, only 24% of the estimated people living with HIV (PLHIV) are on treatment by end of 2020, and no data about PLHIV with suppressed viral load (WHO, 2020)

So, this study aimed to detect and estimate the viral load as predicting factor for treatment failure for adult HIV-1 patients who were on antiretroviral therapy for 12 3 months at different Voluntary Counseling Testing and treatment centers (VCT/ART) in Khartoum State, Sudan

Objectives:

This study aimed to detect antiretroviral treatment failure in adult patients with Human

Immunodeficiency Virus-1 (HIV-1)on anti-retroviral therapy for 12±3 months in Khartoum state, Sudan

Methods

Study population, area, and duration

The study was descriptive cross-sectional health facility-based. It was conducted on 110 adults (≥18 years) HIV-1 patients attending four VCT/ART clinic 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 and the sample size was determined according to World Health Organization indicators to monitor HIV drug resistance prevention at antiretroviral treatment sites (UNAIDS, 2010)

Ethical consideration:

Scientific and ethical approval for this study was granted by the Central Institutional Review Board of Al Neelain University (NU-1RB-17-12-12-112)

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.

Exclusion criteria:

- Patients who transferred out before the date of first scheduled or expected clinical consultation after ART initiation.
- Patients who stopped ART before the date of first scheduled or expected clinical consultation after ART initiation.
- Patients for whom any of the following crucial information is missing; Patient ID and ART initiation date.

Blood samples collection, HIV-1 detection, and quantification

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

One ml of plasma was taken for HIV-1 RNA viral load quantification by multiplex real-time PCR, Cepheid Xpert HIV-1 viral load plasma assay (Cepheid, Inc., Sunnyvale, California, Santa Clara), according to manufacturer instructions, which had sensitivity above 95% in treatment failure detection(Nash et al., 2018)

Data Analysis

Data were analyzed by the SPSS program version 23

Frequencies of patients distribution on VCT/ART, age, gender, patients on first and second lines of treatment, and WHO clinical stages are estimated

Cross tabulation to detect the relation between a viral load that detects the virologic failure and other variables was assessed

Results

Of the 110patients that met the inclusion criteria, the majority of the patients belong to Omdurman VCT/ART center 60% (66/110), followed by Khartoum teaching hospital VCT/ART center 18.2% (20/110), Bahri teaching hospital VCT/ART center 16.4% (18/110) and Elban Gadeid VCT/ART center 5.5% (6/110).

The age of the patients ranged from 19-70 years old with 39.3 years mean57.3% (63/110) were males and 42.7% (47/110) were females. 95.5% (105/110) were in the first line of ART (tenofovir (TDF), lamivudine (3TC) and efavirenz (EFV), and 4.5% (5/110)on the second line (lopinavir posted by ritonavir). The majority of the patients were on stage 3 according to WHO clinical staging 54.5% (60\110), followed by stage 1, stage 2, and stage 4 with frequencies of 22.7% (25/110), 19.1%(21/110) and3.6% (4\110)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 represented 38.2% (42/110) followed by 36.4% (40/110) less than 40 copies/ml,

18.2% (20/110) more than 1000 copies/ml, and 7.3% (8/110) had VL 40-1000 copies/ml. (Figure 1).

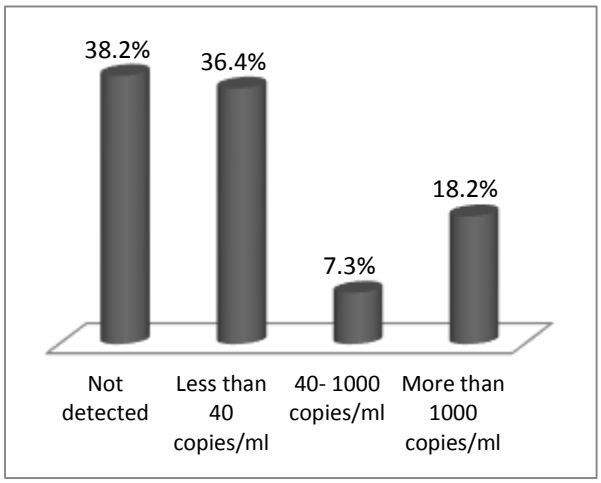

Figure 1: HIV-1 viral load results of patients (n=110) on ART 12±3 months attending VCT/ART units, Khartoum-Sudan

Out of the 18.2% (20/110) 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)] were from the 39-48 years old age group and the majority of them [55% (11/20)] were stage 3 according to WHO clinical staging.

Discussion

Our study evaluated virologic failure in HIV-1 patients on a treatment program for 12+/- 3 months using Gene Xpert which was approved by WHO and introduced as a tool for TB/ HIV-1 diagnosis and monitoring respectively.

The distribution of our study population varies according to the total patient number of HIV-1 patients in each VCT / ART center in Khartoum state.

Some studies have examined predictors of virologic failure among patients failing first-line regimens. For example, a study conducted in South Africa in 2018, showed that the percentage of patients on the first line of treatment had a virologic failure incidence of 22% (Hermans et al., 2018). Other studies in Cameroon with 17% (Tchouwa et al., 2018) and 16% from a systematic review in sub Saharan Africa (Ayele et al., 2017) are resulted in closer results to our finding.

Also, the low number of unsuppressed viral load patients was indicated in studies done in and Uganda in 2015 (Bulage et al., 2017) where the percentage of failure was 11% although its frequencies of HIV infection is higher than in Sudan.

Regarding sex status, the number of males was higher than females (57.3% versus 42.7%) in this study which may be due to those men may be more likely than women to be drug injectors, and more likely to get unprotected sex, which is similar to an earlier study done in Sudan in 2015 in which males were higher (Osman et al., 2017), and dissimilar to a study done in Ethiopia in 2019 in which the females were higher in number (Getaneh et al., 2019).

Our unsuppressed HIV patients were mainly in stage 3, which could be caused by patient-level factors such as lack of awareness of their HIV status or barriers to accessing care such as stigma, high costs, or distance from clinics.

Among patients with virologic failure, 50% are males and 50% are females which shows that gender was independently associated with virologic failure.

The virological failure in our study was observed in the age group 39-48 years, which may be related to the difference in pharmacokinetics and body immunity among different age groups. In addition, the elder usually knew little about AIDS and had poor drug compliance (Yoshikura, 2019), which all contributed to the occurrence of resistance.

Most of our patients (74.6%) had suppressed viral load (non-detectable copies/ ml and less than 40 copies/ ml). The reason is that viral loads won't be detected after 12±3 months of successful treatment, so patients retained in clinical care can achieve, or even exceed current viral suppression levels. This was strong evidence of good adherence and persistence through 12

months of ART access. Patients with unsuppressed viral load may need good adherence or may have metabolic problems or drug resistance mutations a matter that deserves further investigation. Overall these findings put Sudan closer to the UNAIDS treatment target of 2020 in which 90% of patients under treatment must have suppressed viral load.

One of the major limitations of this study is that it did not cover a large number of participants due to financial issues.

Conclusion

Although the sample size of this study did not represent the whole population of HIV patients in different areas of Sudan, it highlighted the presence of treatment failure among HIV -1 patients in the country, since it was associated with a lower prevalence of drug resistance in low and middle-income countries (LMIC), and is recommended as the preferred strategy for monitoring ART effectiveness.

For the improvement of early treatment failure detection, consistent resources that support routine viral load monitoring in Sudan and other resource-limited settings are needed, also establishment of a good treatment program and routine and regular patient follow-up can decrease the virological failure and improve treatment outcomes.

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