

Non-adherence to Highly Active Antiretroviral Treatment: Review

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Abstract: *Background and aims:* This review aimed to describe factors associated with HAART non-adherence and did focus on the HIV/AIDS situation and antiretroviral therapy. *Methods:* The strategy of this review adopted a critical approach to reduce the bias of published or non-published information. Only evidence-based information was used from PubMed, Embase, Medline, and Google scholar. However, relevant grey information from monography/technical reports or specific books was also used. *Results:* Findings were out lighted across the global status of HIV epidemic, HIV/AIDS epidemic in Sub-Saharan Africa, history of HIV and ART in South Africa, HIV infection and antiretroviral therapy, HIV life cycle, HIV treatment, Highly Active Antiretroviral Therapy, Adherence to HAART, and factors associated with HAART non-adherence. The reviewed literature revealed consistency in important factors associated with HAART non-adherence across multiple settings and countries. *Conclusion:* This review was to determine factors associated with non-adherence with highly active antiretroviral therapy among HIV-infected patients attending Lerato clinic in Gauteng, South Africa. The reviewed factors leading to non-adherence will be submitted to policymakers, health care workers in general, and Family medicine staff in particular.

Keywords: Barriers to HAART, ARV, HIV Treatment, Antiretrovirals

1. Introduction

Antiretroviral therapy is a lifelong commitment for patients requiring full adherence to the prescribed treatment by the health care provider. Today, it is well established that Highly Active Anti-Retroviral Therapy (HAART) is provided in large-scale programs which have expanded and matured in Sub-Saharan Africa and attention has shifted to the broader set of long-term challenges in sustaining a vast and complicated public health endeavour [1].

In today's world, The Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS)

have become one of the major global public health problems in many countries, and have claimed more than 36.3 million (27.2–47.8 million) lives so far [2].

This review aimed to describe factors associated with HAART non-adherence and did focus on the HIV/AIDS situation and antiretroviral therapy.

2. Materials and Methods

The strategy of this review adopted a critical approach to reduce the bias of published or non-published information. Only scientific valid information (evidence-based) was used

from PubMed, Embase, Medline, and Google scholar. However, relevant grey information from monography/technical reports or specific books was also used.

3. Results and Discussion

Findings were out lighted across the global status of HIV epidemic, HIV/AIDS epidemic in Sub-Saharan Africa, history of HIV and ART in South Africa, HIV infection and antiretroviral therapy, HIV life cycle, HIV treatment, Highly Active Antiretroviral Therapy, Adherence to HAART, and factors associated with HAART non-adherence.

3.1. Global Status of HIV Epidemic

In recent history, besides COVID-19, the HIV epidemic is one of the worse if not the biggest public health challenges the world has ever seen. In 2020, it was estimated approximately 37.7 million people across the globe were living with HIV. [3].

It is also estimated that more than 2 million people are HIV infected in Europe, especially the Eastern part of it [1].

At the same moment, the number of AIDS-related death also is declining, in 2020, AIDS-related deaths have been reduced by 65% and new infections have been reduced by 54% since 2002. With this, eight countries only have surpassed the UNAIDS “90-90-90” 2020 testing and treatment targets, maybe because of the COVID-19 pandemic, it is not clear if this will lead to an increase in AIDS-related deaths and infections [4].

There is a systematic review done in 2014 on adherence to HAART by Nachege *et al* [5], where they found that in developing countries, the employment status was directly related to adherence to ART, besides other barriers.

A study was done in the USA, for 4 years, by Crim SM *et al* [6] found among younger Hispanic/Latino MSM that forgetting to take their medication was the main barrier.

There is also another study done in New York (2020) with formerly incarcerated people on HAART. They found many challenges to HAART adherence among those individuals that included “forgetting to take medication, pill burden, mental health difficulties, and interrupted regimens resulting from illicit drug use” [7].

3.2. HIV/AIDS Epidemic in Sub-Saharan Africa

The 2020 UNAIDS reports confirm that the majority of people living with HIV are located in low and middle-income countries, especially East and Southern Africa remain the most affected region in the world, with 20.6 million people living with HIV and 670,000 new HIV infections in 2020 [8].

A systematic review done on adherence among adolescents in low and middle-income countries by Ridgeway K. *et al.* (2015) [9] showed significant non-

adherence for patients with the following characteristics: low level of education, unemployed, and abuse of substances including intravenous drugs.

There is also a study done in 2012 by Mendelsohn J. B. *et al.* [10] on conflict-affected and forcibly displaced population in 13 countries, where they were not enough evidence suggesting that HAART adherence and treatment outcomes among conflict-affected and forcibly displaced adults would be as good as outcomes attained in unaffected population groups.

3.3. History of HIV and ART in South Africa

In South Africa, the first diagnosed case of AIDS occurred in December 1982 [11].

The first ART regimen was approved by the United States Food and Drug Administration (FDA) by the end of 1995 and made available to the American public shortly thereafter. In contrast, widespread implementation of ART programs in South Africa did not occur until April 1st, 2004. During 2009, when Mr. Jacob ZUMA became President, and the appointment of Dr. Aaron Motsoaledi as South Africa’s Minister of Health, new attention and urgency was given to the HIV situation in South Africa [12].

After Dr. Motsoaledi acknowledged that the past 10 years were spent “pedalling backward”, the president declared World AIDS Day 2009 as, “the day on which we start to turn the tide in the battle against AIDS” [12].

There is a cohort study done in South Africa in 2011 by El-Khatib Z. *et al* [13] on Adherence and virologic suppression on pregnant women on ART, where they found the main reasons for incomplete adherence were being away from home, busy with other things, forgetting to take their medication, lower level of education, and lack of financial support from partners.

3.4. HIV Infection and Antiretroviral Therapy

3.4.1. HIV Life Cycle

Normally, the immune system, known as T-lymphocytes or CD4 cells, is attacked by HIV which attaches itself to it and migrates inside it. Once in the cell, the virus replicates and in the process, kills the host CD4 cell, thus resulting in a weakening of the immune system. This process is known as the HIV life cycle [14].

The progression of this disease can take many years, during which individuals may or may not experience symptoms. To protect the immune system, antiretroviral treatments employ various strategies to block HIV reproduction at different stages of the cycle. This reduces HIV replication in the body and prevents the virus from advancing to AIDS. This adds further stress to the already weakened immune system.

3.4.2. HIV Treatment

HIV treatment involves taking medicines that slow the progression of the virus and suppress the virus in the body. If untreated, most people infected with HIV eventually develop AIDS over time and may die.

3.4.3. Highly Active Antiretroviral Therapy (HAART)

The combination drug therapy against HIV is called highly active antiretroviral therapy (HAART). It is most commonly done with the combination of three different medications [15].

There are currently six different classes of HIV drugs [15]:

- 1) Nucleoside reverse transcriptase inhibitors (NRTIs)
- 2) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- 3) Protease inhibitors (PIs)
- 4) Integrase inhibitors (INSTIs)
- 5) Fusion inhibitors (FIs)
- 6) Chemokine receptor antagonists (CCR5 antagonists).

Each class of drug attacks the virus at different points in its life cycle as the virus infects a CD4+ T lymphocyte or other target cells. The combination therapy generally includes at least two, and preferably three, different antiretroviral drugs from two or more different drug classes [16].

The selection of individual agents for an optimized background regimen should be based on the antiretroviral treatment history, genotypic and/or phenotypic resistance results, drug-drug interaction potential, and medication intolerance, to maximize antiviral activity and adherence [15]. The primary goals for antiretroviral therapy (ART) are to reduce HIV-associated morbidity and prolong the duration and quality of survival, restore and preserve immunologic function, maximally and durably suppress plasma HIV viral load, and prevent HIV transmission [16].

Drug resistance is one of the main issues related to HAART. Virus strains with reduced sensitivity to zidovudine, the first drug used to treat HIV infection, were first observed in 1989, three years after it was introduced [17].

3.5. Adherence to HAART

According to several studies, people do not like taking medications and have an often-skeptical attitude towards them, and it is known that a negative or skeptical attitude towards medication is often related to poor adherence where the word adherence is preferred by healthcare providers, instead of words like compliance, as it indicates that the treatment plan is based on alliance or a contract between patient and physician, rather than patient passively following physicians' orders [18].

Poor adherence to HIV treatment is associated with reduced efficiency of viral suppression and increased risk of opportunistic infections, which may lead to progression to full-blown AIDS and mortality.

3.6. Factors Associated with HAART Non-adherence

In Sub-Saharan Africa, there are some epidemiological studies like the one done by Erlwanger AS. (2017) [19], where they reported high levels of ARV nonadherence rate (13% to 59%) among countries in this region. A similar study was done by Gary FA. (2015) [20] in Eswatini (Swaziland) with HIV pregnant women, where they found that the

nonadherence level was also high (50%).

At the individual level, ART nonadherence is associated with age, gender, hunger, length of time taking ART, smoking status, alcohol use, depression, income, perceived stigma, and educational level [21].

At the household level, ART nonadherence is associated with food insecurity, socioeconomic status, disclosure, family support, and family size [21].

At the community/institutional level, ART nonadherence is associated with an area of residence, proximity to a clinic or health facility, transportation to a health facility, insufficient health care, and maltreatment at health facilities [22].

There is a case-control study done by Dewing et al. (2015) [23] where they investigated structural and individual level barriers to ART adherence among HIV-positive individuals in Cape Town, South Africa. In that study, barriers to ART adherence were assessed using four measurement tools including a Structural Barrier to Medication-taking Scale, a Substance Abuse and Mental Illness Screener, a Structural Barriers to Clinic Attendance Scale, and a Life Windows Information-Motivation-Behavioural Skills ART Adherence Questionnaire. ART nonadherence was measured from medical records using the pill count method. ART nonadherence was defined as taking less than 95% of doses since the last pharmacy visit or scheduled clinic-visit dates (>3 days late).

4. Conclusion

The reviewed literature revealed consistency in important factors associated with HAART non-adherence across multiple settings and countries. Furthermore, it was evident that HAART remains the mainstay in the treatment of HIV/AIDS.

This review was to determine factors associated with non-adherence with highly active antiretroviral therapy among HIV-infected patients attending Lerato clinic in Gauteng, South Africa.

While previous studies have investigated numerous factors associated with ART non-adherence, studies published to date have had methodological limitations.

The reviewed factors leading to non-adherence will be submitted to policymakers, health care workers in general, and Family medicine staff in particular.

Conflict of Interest

The authors declare no conflict of interest.

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