



Barriers in Access and Adherence to Antiretroviral Therapy in Developing Countries

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I. Abstract

Developments in antiretroviral therapy (ART) are one of the most effective ways of treating individuals infected with HIV and lowering their level of infectiousness. This therapy has been proven to significantly lessen HIV mortality rates through its combination of medicines that aim to suppress the progression of HIV throughout the body. Taking this into account, it's critical that patients adhere to their treatment regimen in order to obtain better outcomes and control the rate of the virus within a population. This paper includes several research studies that indicate patient adherence to antiretroviral therapy and rates of retention to be suboptimal in developing regions of Africa, India, and Latin America. Placing emphasis on the importance of treatment, this paper elaborates on the extent to which barriers, such as country access to healthcare, costs of treatment, perceived discrimination, social stigma, and religion affect patient adherence to antiretroviral therapy in resource-limited environments. Furthermore, identifying the impact of lack and unequal access to healthcare and medications pose itself as one of the most significant obstacles promoting poor treatment adherence. Thus, this paper offers suggestions that can be taken to improve adherence among HIV-infected individuals and alleviate the barriers associated with the uptake of antiretroviral therapy, in order to collectively defeat the growing HIV/AIDS pandemic.

II. Introduction

HIV (human immunodeficiency virus) is the causative agent of acquired immunodeficiency syndrome (AIDS). HIV/AIDS is a growing public health concern in developing countries. Over the last several decades, HIV has compromised the lives of thousands in low income countries. In 2021, sub-Saharan Africa accounted for approximately 67 percent of people of all ages living with HIV and 88 per cent of children and adolescents living with HIV worldwide.³ As the epidemic progresses, these countries face challenges not only from rapid virus spread but also from adverse socioeconomic conditions among many patients with HIV/AIDS.

Antiretroviral Therapy (ART) has been introduced as a treatment for people infected with HIV. It involves the combination of several antiretroviral medicines to suppress the rate at which HIV replicates throughout the body. This has shown to improve the quality of life for people living with HIV by dramatically reducing morbidity, mortality, and the infectiousness of people with HIV. People are able to live worry-free lives once they reach below detection levels with the use of ART as an effective treatment. The advancements in the efficacy of antiretroviral therapy has extended the survival for HIV-positive patients. As a result, adherence and access to this drug therapy is a key component for positive patient outcomes. However, the expansion of ART has not proceeded as quickly as anticipated or expected in global targets set for 2020. In 2018, there were an estimated 1.1 million new HIV infections in the African Region⁴. Limited access to the treatment in developing countries has also proved to lead to suboptimal adherence levels and a greater rate of mortality related to HIV.

In developing countries, ART adherence and rates of retention face challenges from multiple variables such as poverty, social stigma, financial constraints, and medical mistrust. Despite the favorable short term data from low-income countries, concerns exist for suboptimal long-term adherence because of these barriers. Adherence is necessary for sustained viral suppression, preventing disease progression and drug resistance. For this reason, it's vital that individuals in developing countries have access to ART, as well as educating HIV-positive patients on the importance of adhering to treatment.

In addition to this, ending HIV/AIDS as a public health threat includes reaching the 90-90-90 target set by WHO to ensure successful treatment for millions of people.⁵The aim of 90-90-90 targets is to diagnose 90% of all HIV-positive persons, provide antiretroviral therapy for 90% of those diagnosed, and achieve viral suppression for 90% of those treated by 2020.⁶ This is estimated to result in 73% of people with HIV achieving full viral suppression. By further supporting individuals living with HIV in resource-limited countries, we are better able to combat barriers and achieve promising results.

There are a wide array of factors that may hinder ART efficacy in developing countries. Hence, it's crucial that the factors that lead to non-adherence are accurately identified and methods are developed in order to improve adherence to ART overall. The aim of this review is to provide an overview of barriers that prevent or restrict the access to ART and leading to suboptimal adherence rates in developing countries.

III. Adherence Statistics

Developing Countries	Individuals living with HIV virus	Adherence to ART	Non-adherence to ART	HIV prevalence
Peru	110,000 individuals ⁷	60% ¹¹	40% ¹¹	0.4% ⁷
India	2.5 million individuals ⁸	77% ¹²	23% ¹²	0.2% ⁸
Mozambique	2.2 million individuals ⁹	70% ¹³	30% ¹³	11.6% ⁹
Ethiopia	610,000 individuals ¹⁰	73.3% ¹⁴	26.7% ¹⁴	3.0% ¹⁰

IV. Developing countries' health care and access to ART.

There has been notable progress in providing universal care for HIV/AIDS patients in resource-poor countries. Created in 2002, The Global Fund aims to finance the expansion of AIDS treatment in developing countries.¹⁵ However, the lack of qualified human resources and

infrastructure in these countries presents a significant barrier to universal access to HIV care. According to the World Health Organization, the number of physicians working in resource limited countries is low.¹⁶ The most qualified health personnel in resource limited settings live in urban rather than rural areas. Hence, HIV-positive individuals in rural areas are at a significant disadvantage to receiving the best care possible due to the lower availability of medical personnel. There also exists highly active antiretroviral therapy (HAART), which is a treatment regimen typically consisting of a combination of three or more antiretroviral drugs. HAART involves the use of multiple drugs to suppress HIV replication. According to one study in rural areas of Burkina Faso, the responsibility of monitoring HIV-infected patients under HAART falls on nurses, who often have to rely on clinical criteria for efficacy and toxicity monitoring.¹⁶ Additionally, due to the limited number of fully qualified practitioners, there's a low quality of patient care. There is a desperate need to establish basic infrastructure for safety and immune monitoring for patients in underprivileged rural areas. In rural areas of Burkina Faso, access to health establishments with such monitoring facilities is limited, especially for women and during the rainy season. Subsequently, strengthening the health system and resources should be viewed as essential to improving the fight against HIV/AIDS, especially in developing countries where resources are limited.

In addition, the Africa region has one of the largest HIV epidemics globally with 37.9 million PLHIV (people living with HIV) at the end of 2018.⁴ In present time, this is continuously growing with expansion of population and economic instability within the country. The African region also currently accounts for almost two thirds of new HIV infections globally.⁴ Consequently, they have the largest public ART programme in the world and began adopting the policy to offer 'universal access' to ART. However, even with efforts for treatment availability, South Africa has failed to achieve the UNAIDS 90–90–90 targets for epidemic control and has the highest number of new HIV infections per year. This can be seen in the challenges HIV-positive patients face when receiving ART at local hospitals. It raises concerns over the influence and potential decrease in treatment adherence in these areas. One study describing the challenges faced by patients on ART in Vredenburg found that poor treatment literacy, dissatisfaction about the quality of the ART services provided, and the lack of confidentiality in the handling of patients' HIV results were reported as major concerns in obstructing medication adherence.¹⁷ Moreover, another study conducted in Tanzania found that long waiting hours (>10 hours) in a hospital setting, reduced clinic attendance and consequently hindered adherence to ART.¹⁸ Concluding that factors such as poor literacy, lack of confidentiality, wait time, play a critical role in patients want to adhere to treatment.

In many developing countries, there is also a high rate of poor relationships and reported conflicts with medical staff. Studies from Tanzania, Zimbabwe, and South Africa have shown that poor relationships between clinicians and patients actually have a negative impact on drug adherence. This can be seen in HIV-positive males in rural Mozambique, who focus on the lack of confidentiality and poor treatment by hospital staff.¹⁹ Because clinical sites in rural Mozambique are small, patient confidentiality is difficult to maintain. Furthermore, healthcare workers report language barriers and issues with patients being overwhelmed with the information provided to them.¹⁹ The larger language barrier in these countries hinders effective communication between the provider and patient and poses a challenge to ensuring that the patients are aware of the importance of ART or how to take it properly. This can be seen from a

testimonial from a man in Namacurra who stated that “they [healthcare workers] explain things in Portuguese in the hospital. The only things we know how to say are head and belly [in Portuguese]. Sometimes when we have chest pain, we say we have belly pain because we don't know how to say "chest." When we have ear pain, we say "head" because we don't know how to say "ear" and the nurse gives us a prescription that functions for my complaint.”¹⁹ Communication between patient and clinician is a critical component in improving service quality and, in turn, ensuring adequate ART adherence in developing countries.

V. Financial Costs of ART

As the HIV/AIDS epidemic has evolved, the gap has widened between available resources and the needs for care, which may be limited by financial constraints of the patient. Even though different agencies offer international funding to assure increasingly adequate coverage for ART in developing countries, concerns continue to rise on how long this funding will last. Hence, a number of resource-limited countries charge an out of pocket contribution from HIV patients. According to one study, Adult HIV/AIDS patients in 2010 in Burkina Faso were expected to pay a contribution to receive care, as well as pay \$2.51 USD monthly to receive antiretroviral drugs from the government.²⁰ Prior to 2001, the annual cost of receiving ART for a patient in a resource-limited country was estimated to be \$10,000 to \$25,000 USD.²¹ There are also a variety of direct and indirect costs for patients seeking ART, such as transportation to treatment facilities and loss of working days for attending appointments. According to another study, many respondents missed hospital appointments and/or their doses either because they were unable to raise enough money for transport fares or because they forewent buying medicine in order to buy necessities such as food.¹⁷ Financial constraints heavily impact HIV positive patients living in socioeconomically challenged countries, contributing to a lack of treatment follow-up and adherence by patients.

VI. Interruption of supply to ART

Disruptions in HIV services consist of limited access to ART drugs, HIV testing, psychological or counseling sessions, etc. They severely impact ART continuity in developing countries. Treatment interruption (TI) compromises treatment success, after which viral load will typically increase to pre-ART levels in 4 weeks, thereby increasing the risk of transmission and HIV mortality rates.²² TI can also induce antiretroviral drug resistance and have detrimental effects on CD4+ immune cell count and clinical progression.²² One study compared a projection of COVID-19 deaths under reasonable worst-case scenarios and HIV deaths over five years and found that an interruption for more than 6% of individuals on ART for 9 months could cause the number of HIV deaths to exceed or match the number of COVID-19 deaths.²³ This is detrimental for countries in Sub-Saharan Africa, specifically South Africa, which would experience the most substantial changes in HIV incidence and mortality due to the country's higher HIV incidence rate and high percentage of HIV-positive people living on ART. Thus, it is essential that maintaining and adhering to ART treatment should be the utmost priority during any health system disruption that may occur.

VII. Lack of information and education on ART

In developing countries, economic demands and poor rural education infrastructure have converged to produce a large population of individuals who have low literacy. According to the World Bank, sub-Saharan Africa has the lowest adult literacy rate worldwide, with 60% of its population age 15 and over able to read and write, which is far below the global percentage of 80%.²⁴ Furthermore, sub-Saharan Africa has the highest rates of education exclusion, with 60 percent of the youth between ages of 15 and 17 not in school.²⁵ As a consequence, there is little to no education about ART nor advocacy for the treatment, which results in many HIV-positive individuals in rural areas remaining unaware of ART and its beneficial effects. A study that examined patients' literacy and education around ART adherence in an urban treatment center in the Gambia showed that formally educated patients were significantly more likely to achieve virological suppression at both six and 12 months.²⁶ Literate patients had similar benefits at 12 months, with improved virological outcomes associated with degree of literacy.²⁶ Patients from urban areas have easy access to information about the importance of strict adherence to ART, and may have good educational status. A study also identified that the odds of adherence among HIV-positive patients in South Western, Ethiopia who were unable to write and read were almost 90% times lower compared to those HIV-positive patients with higher educational status.²⁷ This relation to education shows that patients with good educational status, such as high literacy rates, are better at adhering to those with poor educational status.

VIII. Stigma and Discrimination

Advances in treatment, such as ART, have transformed the lives of many HIV-positive patients throughout the world, but integration and acceptance of these individuals in societies within developing countries has not improved as dramatically. Many people living with HIV noted that family and friends behave differently toward them after learning they have the virus. One study said that 71% of its survey respondents who gave incorrect answers about HIV transmission said they would be uncomfortable having their food prepared by someone who had HIV, while 40% of those who gave correct answers said they would be.²⁸ This stigma significantly damages relationships with HIV-positive individuals. To avoid the unpleasant consequences of revealing their status, many HIV-positive patients even choose to conceal their seropositivity to others. The fear of being victimized and/or rejected by their family or community generates a fear of exposure, which in itself affects adherence. Furthermore, one cross-sectional study of 300 outpatients from the largest ART clinic in Botswana showed that non-disclosure of seropositivity to one's partner was associated with increased odds of non-adherence.²⁹ HIV-related stigma in societies around the world compromises ART adherence to a large extent.

Discrimination is also manifested toward HIV positive individuals and the integration in their own culture and religion. According to a study, shame-related HIV stigma is strongly associated with religious beliefs such as the belief that HIV is a punishment from God or that people living with HIV/AIDS have not followed the Word of God, which is widely held in many cultures.³⁰ This belief was shown to be significantly higher in rural areas of South Africa. Furthermore, most participants (84.2%) said that they would not disclose their HIV status to their pastor or congregation if they became infected.³⁰ This supports the statement that the influence that religious beliefs have on HIV-related stigma is significant. Furthermore, it makes the HIV patient less willing to disclose their status in fear of being ostracized from their religious groups.

By supporting the stigma, it can lead to feelings of shame, fear of disclosure, isolation, and despair. These feelings can keep people from getting tested and treated for HIV.

IX. Religious attitudes towards HIV

Furthermore, attitudes about health and medication resulting from spiritual and religious beliefs have impacted patient adherence to HIV treatment. This influences how HIV patients understand health concepts, how they take care of their health, and how they make decisions about their health. In sub-Saharan Africa, Pentecostal churches are currently among the fastest and largest growing Christian movements.³¹ According to one study, five of the 18 female respondents reported ceasing taking ART because they believed that either God or ART drugs had cured their HIV infection.³² Three female Pentecostal Christians reported that they had been cured by God and added that their pastors asked them to stop taking ART drugs, therefore they had no need to continue taking ART.³² For Hindus and Muslims, religious activities and festivals, such as Teej and Ramadan, play a significant barrier to the patient's adherence to ART treatment due to the obligation to fast and abstain from drinking or eating. Moreover, some faith-based institutions have contributed to misinformation about ART. A study from sub-Saharan African countries confirms that pastors claim to provide complementary therapy to HIV through prayers, holy tea, holy water and other faith-based healing rituals.³¹ These traditional remedies and rituals, as well as influence from these beliefs are known to be barriers to ART adherence and undermine the efforts from healthcare professionals to initiate and continue treatment in people living with HIV.

X. Adverse effects of drug therapy

In addition to stigma, the reality of the drastic side effects associated with ART is one of the most significant obstacles faced by many people living with HIV. Adverse effects have been reported with the use of antiretroviral (ARV) drugs, including vomiting, nausea, diarrhea, severe headaches, kidney, liver, or pancreas damage, and severe headaches.³² Other side effects from some HIV medicine can also lead to problems that may not appear until months or years after initiating ART. A qualitative cross sectional study conducted in Uganda revealed six of its respondents reported that experiences or fear of severe treatment side effects led to their non-adherence to ART.³³ The severity of ART side effects led individuals to discontinue the treatment and seek relief. The majority of HIV-positive patients hear about the severe treatment side effects from friends who have such experiences, ART adherence education sessions from health workers, and from radio programs.³³ Additionally, a recent review stated that ART adherence was significantly lower among patients with side effects than among patients who reported no side effects.³² The side effects of taking ART are a significant factor in poorer medication adherence amongst people living with HIV and discontinuation of their ART regimen overall.

XI. Future Projections

By acknowledging these barriers, resource-limited countries are better able to enact facilitators that lead to success in the adherence of ART, as there is still a need to promote access to ART in underprivileged areas. There have been significant efforts and achievements in decreasing the cost of ART and HIV testing, thus improving adherence to ART. This includes

the introduction of nurse-based counseling intervention (AIMS), which involves the promotion of self-management guided by a review of electronically collected medication adherence data.³⁴ A 15-month effectiveness study with 21 nurse providers across 7 clinics in the Netherlands stated that treatment arm participants demonstrated significantly superior HIV outcomes compared to those in the control arm.³⁴ Moreover, a cost-effectiveness analysis suggested that AIMS saves society \$664.61 (€592) while adding 0.034 quality-adjusted life years per patient.³⁴ Studies also show that there is a development of process chemistry improvement to ART drug manufacturing by generic companies, reformulation, dose optimization, and extension of shelf life.³⁵ According to another study, there is also a new pharmacological development that has been that of nanotechnology to develop long-acting injections of antiretroviral drugs that could be administered once monthly.³⁵ Taking this into account, resource-limited countries are able to expand their access to ART through their widespan accessibility to the treatment and lower HIV mortality rates in their population. However, current and future challenges include the continued globalization of ART through scale-up and continued improvements in cost efficiency, engagement and retention of patients in care, new immunological and pharmacological approaches to prevention and HIV suppression.

XII. Conclusion

Adherence remains the primary obstacle to optimal outcomes among those engaged in treatment. A variety of barriers reduce adherence to ART in developing countries. Many studies deem that poor quality of healthcare, lack of infrastructure present, financial costs of the treatment, lower literacy rates, and interruptions in ART supply within the country itself present themselves as wide-scale barriers. Other studies also state that individual level barriers include HIV-stigma and discrimination, the lack of information on ART, and the adverse effects of the treatment. These factors promote the rate of failure to adhere to treatment, which is then associated with less effective viral suppression. This puts the health of the HIV-positive individual at risk and also creates treatment resistance. Thus, governments and healthcare systems should prioritize programs to mitigate these barriers and improve adherence. Otherwise many ART programmes in developing countries will fail.

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