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Review Article

Efficacy of viral load suppression on life expectancy of human immunodeficiency virus patients: a literature review

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ABSTRACT

In a bid mitigate the spread of HIV and AIDS since it was diagnosed, several interventions ranging from palliative care, increased access to HIV treatment to manage opportunistic infections and the current drive of improving clinical outcomes through suppression of viral load are all aimed at prolonging survival of HIV and AIDS patients. The authors endeavour to corroborate the effect of viral load (VL) suppression on ART HIV patients. The authors applied a comprehensive search by merging terms for survival of HIV patients to clinical, demographic and socio-economic factors in NCBI and MEDLINE databases. About 15 articles were considered by outlining research questions, generating key words and search terminologies. Only articles published since 2013 during scale up of VL interventions were considered. It is worth noting that unsuppressed VL clinically decisively causes death in HIV/AIDS patients, propelled by a number of associated causes including opportunistic infections (OIs) Tuberculosis (TB), Non communicable diseases (NCDs), age, sex, income, geographic location among others. Whereas there is marked decline in risk of dying among HIV/AIDS patients resulting from VL suppression, other factors including; early detection and timely treatment, managing OIs, NCDs and TB treatment, tackling socio-economic barriers and multi-pronged community focused interventions like Community Client Led ART Delivery CCLAD, Community Drug Distribution Point (CDDP) interventions enhance survival of HIV/AIDS patients on lifelong ART.

Keywords: Efficacy, HIV/AIDS, Life expectancy, Viral load

INTRODUCTION

Since the diagnosis of HIV/AIDS in the 1980s, a number of recommendations, guidelines have been constituted to mitigate the magnitude of HIV. As a result, interventions have ranged from: - providing palliative care to HIV infected patients; extending HIV treatment to HIV patients with opportunistic infections, patients in WHO stage III and IV, patients with CD4 T cell count less than 500 and currently HIV viral load less than 200 copies/ml.[1] With current studies indicating that viral load suppression increases survival among HIV patients and having in mind a series of HIV interventions not effectively working, there is need to explore the efficacy of viral load suppression to HIV patients with varying characteristics and exposure factors.[2-5]

For instance, the responsiveness to treatment among HIV patients in rural and urban communities, poor and wealthy households, under developed and developed societies, old and young, different races, sexual orientation among others varies across the board.[7]

Viral load (VL) refers to the amount of HIV in a blood sample reported as the number of HIV RNA copies in a millilitre of blood. Uptake of antiretroviral drugs helps in

the treatment and prevention of HIV infections. The drugs fight virus through interfering or stopping reproduction of HIV in the body system, thus reducing the amount of the virus in the body. The overall aim of antiretroviral therapy (ART) is to suppress the HIV patient's VL to undetectable level, to the extent of the virus not being detected through a VL test. The VL test entails drawing dried blood samples being used in identifying HIV VL with treatment failure limit of 1000 copies/ml. On the other hand, virological failure happens when VL is more than 1000 copies/ml on two consecutive episodes of VL tests every three months with adherence support and six months after initiating on a new ART regimen. Currently, WHO recommends VL tests to be done at six months from the time of enrolling on ART and 12 months thereafter. An HIV patient is considered stable on ART when the following criteria is met: - active on ART drugs for a minimum of a year; not facing illnesses; has good understanding of lifelong adherence coupled with evidenced treatment success, implying two consecutive viral load tests reported below 1,000 copies/ml.[8]

A study by Ford et al, revealed that AIDS-related illnesses and bacterial infections were the leading causes of hospital admission and mortality among adults.[9] The causes among adults included malnutrition, wasting, parasitic infections, haematological disorders in the Africa while respiratory disease, psychiatric disorders, renal disorders, cardiovascular disorders, and liver disease in Europe. Haematological disorders were reported in North America and respiratory, neurological, digestive and liver-related conditions, viral infections, and drug toxicity in South and Central America. Tuberculosis (TB) is reported as the major cause of death among HIV patients in Africa, with mortality being high among adults compared to children. Much as free ART is accessible to most patients, HIV continues to contribute most of the reported deaths. To reverse this trend, there is need to prevent, treat and manage HIV by; use of condoms during sex, early testing, adhering to ART, being faithful to a sexual partner, embracing voluntary medical male circumcision (VMMC) as a prevention measure for negative males among others. It should be noted that people living with HIV often need counselling and psychosocial support, access to good nutrition, safe water and basic hygiene and managing opportunistic infections to maintain a high and long quality life.[8]

To this effect therefore, the authors attempt to substantiate the evidence that viral load suppression entirely determines survival of HIV Patients on ART.

METHODS

Utilizing a comprehensive search approach by merging terms for survival of HIV patients and unsuppressed viral load, other opportunistic infections, age, non-communicable diseases, poverty, geographical location, the authors searched NCBI and MEDLINE through PubMed, PMC, Embase, Google scholar to identify studies reporting VL and survival of HIV patients (Table 1).

The authors focused on articles published from 2013 when VL testing was intensified. Key consideration was given to articles written and/ or translated in English, publications focusing on HIV/AIDS, Viral Load, HIV publications from across the globe, and publications from authentic sources. The key words used included: - HIV, patients, ART, death, survival, poverty, unsuppressed, HIV, AIDS, death, tuberculosis, patient, NCD, OIs, viral load. Articles excluded by the authors included publications before 2013, publications not written and/ or not translated in English, articles not focused on HIV and AIDS, Articles from uncertified sources and articles without author details.

The authors included a total of 15 articles. To obtain the final article number, the author framed the research question, defined key words and search terminologies. Thereafter, the author browsed into NCBI and MEDLINE, selecting the databases (PubMed, PMC, Embase, Google scholar), one at a time, inputting the search terms at different intervals, filtered by date of publication, free full article, human's category and then selecting the article of preference.

RESULTS

Unsuppressed viral load

Several studies reveal that risk of death among HIV patients is highly associated with viral load.[3-5,7] This implies that the longer an HIV patient is on ART and adhering to treatment, the more likely the chances of viral suppression thus low risk of death. According to a series of studies, ART start date, social economic factors, stigma were contributing factors to death among HIV patients.[2-6] However other studies reveal that the sex of an HIV patient did not affect viral load suppression, thus not associated with risk of death. The losses to follow up among HIV patients on ART triggered likelihood of death, given that most of the lost to follow up patients either dropped off treatment, did not adhere to treatment as prescribed by health care workers, leading to unsuppressed VL.[6] Across the globe, for HIV patients to manage HIV associated symptoms and opportunistic infections (OIs), they apply a series of interventions including therapeutic, physical activity, psychological well-being like herbal medicines, faith healing, self-prescription of medicines. As a result, most patients abscond from taking ART thus compromising VL suppression coupled with treatment failure, toxicities resulting from unproven herbal medicines.[10]

It is important to note that VL does not entirely determine death among HIV patients but is a clinically ultimate cause of death among HIV patients. Some studies suggest that mortality among HIV positives is highly associated with several other causes including Tuberculosis, suicide,

geographical location, age, CD4 cell count, mode of transmission of HIV, drug failure, geographical location and HIV/TB co-management.[3-5,7,11] For instance, in Uganda, most key populations including commercial sex workers, men having sex with men, injecting drug users, lesbians, transgender are criminalized populations and thus not likely to freely access HIV and viral load services as recommended. As a result, their adherence levels are compromised, registering unsuppressed viral load, multiple drug treatment failures among others.[4] Other categories of populations like fisher folks, the incarcerated and people in enclosed settings like soldiers, prison officers, adolescent girls and young women tend to have poor adherence to treatment, poor health seeking behaviour, thus compromising their health. It should be noted that men, across the board have a poor health seeking behaviour, no wonder their survival chances are slim compared to women on ART.[5]

Table 1: Search approach.

Natural language	Term mapped to database vocabulary
P (Patient) = Virally suppressing patient	HIV viral load (PubMed, PMC, Embase, Google scholar)
I (Indicator) = Viral load Suppression	Viral load suppression (PubMed, PMC, Embase, Google scholar)
C (Comparison) = HIV patient	VL, OIs, Age, NCDs, Poverty, Residence (PubMed, PMC, Embase, Google scholar)
O (Expected outcome) = survival	Dead, Alive (PubMed, PMC, Embase, Google scholar)

Opportunistic infections

Opportunistic diseases among HIV patients are a result of either lack of immune defences or availability of environmental microbes and pathogens. The common OIs/diseases are: - bacterial (TB, MAC, pneumonia, septicaemia; protozoal (PCP, microsporidiosis, toxoplasmosis, leishmaniasis, isosporiasis, cryptosporidiosis); fungal (candidiasis, cryptococcal meningitis, penicilliosis); viral (cytomegalovirus, herpes zoster); Kaposi sarcoma, squamous cell carcinoma and lymphoma. These OIs continue to cause mortality among HIV patients despite improvements in ART access and management due to poor adherence, treatment failure, unknown HIV status. Amidst the presence of combination prevention and treatment services, HIV patients still manifest severe OIs despite a virological and immunological reaction to ART. The late delayed identification of and management of immune reconstitution inflammatory syndrome has highly resulted into death.[8]

Non-communicable diseases

Non communicable diseases, comprising four types (cancer, chronic respiratory diseases, cardiovascular diseases and diabetes) is the leading cause of death globally, largely among older people and HIV patients. The rates are on the increase in developing countries, majorly due to smoking habits, alcohol abuse, less physical activity, poor diet and partly because HIV management continues to focus on managing acute not chronic diseases. Studies have revealed that HIV patients have a higher risk of cardiovascular disease, cancer, obesity, chronic obstructive pulmonary disease with a steady increase in cases among women, older adults and those with lower education. NCDs were further associated with low CD4 thus persistent inflammation of immune system.[12]

Age and sex

According to Agolory et al, about 50% men and women do not know their HIV status.[13] HIV incidence reported higher among females than males and adolescents have the lowest HIV testing rates. Among the contributing factors for adolescents are inadequate information about access to HIV treatment and prevention, lack of HTS services and settings friendly to adolescents. Among men, stigma, health seeking behaviour, barriers related to socio-economic and health facility dynamics affect their urge to test. Additionally, VL uptake is also low among paediatric and adolescents, partly due poor drug adherence, inadequate ARV formulations that are paediatric friendly, nondisclosure, limited peer support network, stigma, non-compliance to existing guidelines among others.

Other studies consider particular age categories of much priority over others in mitigating death among HIV patients. According Arpadi et al, HIV positive children and infants have a poor viral load suppression compared with HIV positive adults on ART, thus children and infants are more likely to die than the latter. The limitations faced by children and infants as reported by Arpadi et al range from poor health care system, limited allocation of resources to infant and children HIV care including wanton viral load monitoring. Much as life expectancy of adult HIV patients has continued to drop, women have registered more gains than men. This disparity is attributed to: - the difference of HIV mortality across specific age groups; women are more likely to recover from HIV coinfections compared to men; women enrolling for ART more than men.

Geographical location and poverty

Patients in hard to reach locations have a high likelihood of dying compared to patients closer to health facilities

providing ART services. Since the discovery of HIV in the 1980s, the different strategies presented to curb the HIV epidemic have increasingly registered progress. Until the 1990s, HIV patients were majorly provided palliative care until their death. ARVs at the time were very expensive and a preserve of the rich and well positioned in society. Later on, HIV testing was extended to most populations and ARVs provided to the very sick at a free cost. Increasingly, with the increase in funding from the United States Government under the PEPFAR Program, more people continued to access treatment for HIV at zero cost and many more got to test and know their HIV status. This eventually spurred access to HIV care as most health systems were strengthened by accrediting more health facilities to provide HIV, health workers trained on management of HIV using WHO staging guidelines, use of CD4 machines for testing and eventually viral load screening.[8] Using the UNAIDS 90 90 90 approach, more people know their HIV status, the HIV positive are increasingly starting ART, staying on ART, adhering to ART, taking viral load tests and clinically improving. This is resulting from the gains registered and confidence built by different stakeholders with commitment to accelerate HIV epidemic control.[14]

According to Coninck et al, patients recently started on ART in the western world registered lower risk of dying, due to improved health system coupled with good adherence to treatment, timely management of OIs and co-infections, limited access to toxic drugs.[7] Despite this improvement however, these patients are more at risk of dying compared to non-HIV patients.[7] In developing countries like the Sub Saharan Africa (SSA), there is relative efforts needed to bridge the unmet need for ART using different scale up models of testing like self-testing, community outreaches, index testing for the hard to reach populations. The proportion of patients with suppressed viral load is still relatively low partly due to limited coverage and implementation of the UNAIDS 90 90 90 strategy. Without addressing the gaps across the cascade in view of populations in hard to reach areas, mortality among HIV patients will not drop as expected.[15]

DISCUSSION

There is need for managing psychosocial effects and stigma associated with HIV among HIV patients to address suicidal tendencies and adherence to ART for better clinical outcomes. Most facilities in developing countries like hospitals, clinics and other recreational facilities do not accommodate the disabled population, thus limiting them from accessing the most needed HIV services towards improving the survival. Some key populations or most at risk populations like commercial sex workers are criminalized, yet they are more vulnerable to HIV than other populations. This could be achieved by encouraging social network relationships, opening up to trusted family members and peers for financial, material and emotional support. Coupled with self-care, risk reduction and healthy lifestyle practices like regulating number of sexual partners, safe sex practices to enhance psychosocial and physical well-being, patients should be provided with nutritional supplements to ensure good adherence to HIV treatment thus enhancing viral load suppression.

The need for specialized management and prioritization of HIV care for infants, children and adolescents towards improving survival of these populations is overdue. Additionally, special attention to non-communicable diseases among HIV patients to avoid multidrug resistance, unsuppressed viral load, drug adherence and risk of death. For instance, to manage cryptococcal infections, there is need for improving CrAg screening and preventive therapy, a reliable remedy for resource limited settings. Building capacity of healthcare workers about the incidence, diagnostic procedures, clinical symptoms and signs, risk factors and treatment of OIs and immune reconstitution inflammatory syndrome amidst combination prevention therapy. Prevention, timely diagnosis and treatment of OIs like MDRT, PML should be prioritized for better clinical outcomes. To sustainably achieve these results, integrating NCD care in routine HIV management will enhance prevention, awareness among HIV patients and the general population.

Strengthening health care systems across countries to ensure improved quality of health care among HIV patients with varying needs and conditions is necessary. There is need to increase access to HIV testing and treatment points nearer to the people to enable timely monitoring and management of HIV. This will be made possible by increasing coverage of HIV services in hard to reach areas and lower health facilities, multipronged and differentiated service delivery models like CDDPs, CLADS to improve client retention and adherence. Men focused and integrated efforts to enhance their access to HIV services, for instance assisted partner notification, work-based testing, flexi clinic hours friendly for men including weekends, integrated HTS campaigns alongside HIV screening services for NCDs, VMMC, condoms use, will help reverse the epidemic thus improving life expectancy. Scale up of community approaches like home-based, index testing, self-testing, moonlight clinics for key and priority populations. Facilitating campaigns against self-prescription of ART, dependence on herbal medicines will mitigate new infections among virally unsuppressed patients.

Furthermore, routine monitoring of viral load at recommended intervals to ensure right regimens are provided to patients appropriately should be implemented. Increase in funding towards availing implements required in scaling up viral load monitoring and HIV management should be enhanced. By and large, viral load and other factors stated above need to be prioritized by limiting commercialization of HIV by donor communities.

Whereas most HIV patients recognize biomedical measures like VL as a determinant of their health status, side effects of ART they encounter are not prioritized as critical health complications for HIV patients yet regular monitoring of emergencies, drug failure are critical for viral suppression. This will require regular case-based surveillance throughout the continuum of care for better clinical outcomes.

By and large, with advancements in HIV care and treatment, life expectancy has significantly improved among HIV patients. This milestone is noted by the continued decline in risk of dying for HIV patients. Whereas the effect of VL diagnosis on mortality has been recognized, the evidence of its effect on lifelong treatment is not well documented, one aspect the author attempts to contribute to. Therefore, to increase survival among HIV patients, a multipronged approach is required ranging from timely diagnosis and treatment for HIV, reinforcing prevailing recommendations of providing vaccination and chemoprophylaxis against key preventable infectious diseases among HIV patients. These efforts specifically entail managing opportunistic infections, stigma, early start of ART, adherence to treatment, managing TB and non-communicable diseases among HIV patients, addressing psychosocial issues of HIV patients and addressing poverty. The instant ART enrolment under the test and treat model should be boosted by improving quality of counselling, early identification of HIV positives, implementing recency testing, routine clinical contact of health workers with HIV patient, improving electronic and scaling up biometric tracking of patients to inform policy and efficient allocation of resources. Therefore, efficacy of VL suppression on life expectancy of HIV patients is influenced by a combination of varying factors, interventions and circumstances.

CONCLUSION

To assure survival of HIV/AIDS patients on lifelong ART, multipronged and innovative approaches are required that are focused on person centered monitoring, with special attention to individual clinical contact and health outcomes as well as effective TB/HIV co-management. If compounded with quality data that is reliable, accurate, transparent of high integrity for informed decision making; standardizing health data exchange and systems of surveillance; adequate staffing of human resources for health and capacity building; increased health financing to facilitate availability of critical medical supplies and logistics and improved laboratory services to facilitate timely laboratory proficiency testing quality improvement, recency testing, serum CrAg; integrating comprehensive prevention packages like VMMC, virtual elimination/Prevention of Mother PMTCT including comprehensive reproductive, maternal, new born and child health (RMNCH) services; other innovative approaches like the PEPFPAR adolescent girls and young women (AGYW) initiative, CCLAD, CDDP models of care; cervical cancer screening among HIV patients; gender based violence (GBV) prevention and advocacy mechanisms; addressing stigma and targeted interventions for most at risk populations like commercial sex workers, (CSWs), lesbian, gay, bisexual, transgender, queer or questioning, and intersex (LGBTQI) groups; meeting the OVC health, education, safety and economic needs. Without the above mechanisms, interventions and standards being implemented with fidelity and to scale, can the survival of HIV patients on ART be attributed to VL suppression with systematic availability of HIV testing kits, ARVs and commodities; effective linkages of HIV patients; high ART coverage; high patient retention and adherence to clinical guidelines.

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