MAKERERE UNIVERSITY

INFECTIOUS DISEASES INSTITUTE

Delayed Antiretroviral Therapy (ART) Initiation among Hospitalized Adults in a Resource-Limited Settings: *A Challenge to the Global Target of ART for 90 of HIV-Infected Individuals*

Global Commitment on HIV:

The goal is to fast-track the end of the HIV/AIDS epidemic through the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 campaign. That is, to **test** 90% of all people living with HIV, **treat** - initiate and sustain combination antiretroviral therapy (cART) for 90% of all those diagnosed HIV-infected, and have sustained undetectable viral load among 90% of cART-treated individuals. The World health Organization (WHO) "test and treat" guideline for initiating cART among HIV-infected adults irrespective of CD4 counts is aligned to this goal.

The Problem:
There is delay in initiating persons with untreated advanced HIV disease on cART. Second is the failure to sustain cART treatment in resource limited settings (RLS). Lastly, is the fragmented implementation of "test and treat" approaches within the national HIV care program due to poor engagement of HIV-infected adults. The result is (1) onward transmission of HIV (2) unsuppressed viral load among 90% of cART-treated individuals, (3) morbidity and mortality in individuals with advanced disease and opportunistic infections

Finding a Solution:

The UK government through GILEAD Sciences at the Infectious Diseases Institute, and the Uganda HIV/TB COHRE Training Program at Joint Clinical Research Center (JCRC) funded a solution-seeking study. The aim was to generate evidence that would inform health policy and strategies in RLS, for reaching hospitalized HIV-infected adults who are most-at-risk of morbidity and mortality, amidst the wider scale of "test and treat" strategy in many ambulatory HIV care settings.

The Approach:

Across-sectional study was conducted at Mulago National Referral Hospital in Kampala Uganda from December 2012 to March 2013.The period prevalence of cART initiation status in 13 years and older clients, within two weeks of HIV diagnosis and hospitalization was determined using cART initiation status data, CD4 cell count and WHO HIV clinical stage III/IV extracted from patients' charts, for those still hospitalized for two weeks and more, and through phone calls for those that left hospital within the two-week period. Data on date of admission, inpatient diagnosis, CD4 cell count and date of most recent CD4 count (whenever available), opportunistic infections in past and present, Karnofsky performance score, comorbidities, and reasons for delayed cART initiation (for those that did not initiate cART during hospitalization) was collected.

Findings

Delayed cART initiation can lead to death

Out of **289** HIV-infected adults with delayed cART initiation, 94 (33%) died within two weeks due to tuberculosis [31/94 (33%)], Kaposi's sarcoma 10/94 (11%), and bacterial meningitis 9/94 (10%). It is important that this evidence is used to inform national communication strategies for HIV control.

Awareness of HIV-infected status by patients does not necessarily result in linkage to cART

A significant number of hospitalized HIV-infected patients (**76%**) were aware of their HIV-infection status prior to current hospitalization and had received cotrimoxazole prophylaxis but not cART. Overall, 258/386 (66.8%) had visited outpatient clinics five times or more during the year before recruitment to the study, but had not been linked to cART. Patients with CD4 counts above 50 cells/μl and patients living outside Kampala city were more likely to have delayed cART initiation.

Hospitals may be faced with a challenge of adhering to the WHO 'test and treat' program

Hospital settings like Mulago NRH where this study was conducted, may be presenting a challenge of managing advanced untreated HIV disease resulting in a high post-discharge mortality rate. In this study, **75%** of ART-naïve HIV-infected patients delayed to initiate cART within two weeks of eligibility. Patients attributed the delay on long periods (> two weeks) of preparation of cART 54/195 (27.6%) and failure to honor referral appointments (51/195) in hospital settings. To further confirm this challenge, was a prior study on the same wards, which reported that only 62% of surviving HIV-infected participants were linked to HIV care, and only 15% received cART, and 35% died, within six months of discharge from hospital.

Community awareness and knowledge of benefits of timely cART initiation in very sick patients is important

Up to **80%** of patients who died before cART initiation were still in hospital and the main reason for not initiating cART despite physicians' recommendations was postponement (by the patients and relatives). Some caretakers reasoned that patients were 'too sick, or too weak' to be initiated on cART.

Continuous Professional Support for health workers may reduce and reverse delayed cART initiation at hospital level

Mentorship and training support for front-line health care providers to handle cART eligible individuals in hospital settings is important. Emphasis should be on ART-naïve patients who are considered too weak to initiate cART due to ongoing treatment for opportunistic infections.

Outreach Programs may play a significant part in cART linkage programs

Strategies for actively reaching individuals that slip through the ambulatory ART initiation efforts, only to present to hospital settings with untreated advanced HIV disease are necessary. This intervention may reduce mortality in advanced HIV ART-naïve individuals.

Strengthening the national reporting mechanism may reduce loss to follow up and delayed cART initiation

Proactive strategies for cART initiation cannot succeed without a national HIV care database with unique identifiers to track patients between different HIV treatment sites. In this study, cART initiation was simply by patient self-report! Patients recorded as "lost to follow-up" could not be verified as dead or alive or attached to other health facilities thereafter.

Conclusion

In RLS, policy strategies for cART initiation during hospitalization may be best designed and owned at hospital level for better patient outcomes in advanced HIV. Electronic patient tracking tools could improve linkage to HIV treatment programs and prevent HIV/AIDS-associated.

Authors

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