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Implementing Rapid Initiation of Antiretroviral Therapy for Acute HIV Infection Within a Routine Testing and Linkage to Care Program in Chicago

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Abstract

Growing evidence suggests that rapid initiation of antiretroviral therapy for HIV improves care continuum outcomes. We evaluated process and clinical outcomes for rapid initiation in acute HIV infection within a multisite health care–based HIV testing and linkage to care program in Chicago. Through retrospective analysis of HIV testing data (2016-2017), we assessed linkage to care, initiation of antiretroviral therapy, and viral suppression. Of 334 new HIV diagnoses, 33 (9.9%) individuals had acute HIV infection. Median time to linkage was 11 (interquartile range [IQR]: 5-19.5) days, with 15 days (IQR 5-27) to initiation of antiretroviral therapy. Clients achieved viral suppression at a median of 131 (IQR: 54-188) days. Of all, 69.7% were retained in care, all of whom were virally suppressed. Sites required few additional resources to incorporate rapid initiation into existing processes. Integration of rapid initiation of antiretroviral therapy into existing HIV screening programs is a promising strategy for scaling up this important intervention.

Keywords

HIV, acute HIV infection, linkage to care, antiretroviral treatment, HIV testing, continuum of care

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Introduction

Acute HIV infection (AHI) refers to the initial stages of HIV when viral load is elevated and risk of transmission to others is high.[1] Some studies suggest that patients with AHI account for a high proportion of new transmissions.[2-5] Newer testing algorithms allow for earlier diagnosis of AHI with combination p24 antigen, HIV-1, and HIV-2 antibody detection, followed by HIV-1/HIV-2 antibody differentiation assay and polymerase chain reaction testing for viral RNA.[6-9] Detection of AHI is a high priority for screening programs since diagnosis in the acute stage offers the opportunity for rapid linkage to care and initiation of therapy.

Universal antiretroviral therapy (ART) is recommended for all persons living with HIV since it has been shown to confer

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What Do We Already Know about This Topic?

Programs for rapid initiation of antiretroviral therapy for HIV improve time to linkage to care, retention in care, and durable viral suppression, yet have been resource-intensive to implement.

How Does Your Research Contribute to the Field?

Rapid initiation of antiretroviral therapy for HIV can be successfully incorporated into existing programs for routine testing and linkage to care with minimal additional resources.

What Are Your Research's Implications toward Theory, Practice, or Policy?

Routine HIV testing and linkage programs can provide the infrastructure and support to implement rapid initiation for antiretroviral therapy for treatment of HIV and should be considered by public health practitioners as a strategy to scale up this important intervention that will help us achieve the 90-90-90 goals for HIV elimination.

reductions in morbidity and mortality.[10] More recently, studies have shown the benefits of rapid initiation of ART. Within the United States, Hoenigl et al (2016) reported on rapid viral suppression for patients starting ART within 30 days of diagnosis. The San Francisco General Hospital HIV Clinic developed the RAPID (Rapid ART Program for Individuals with an HIV Diagnosis) protocol, offering ART on the same day as the first clinic visit. They found faster time to viral suppression for patients with acute or recent (<6 months) infections who were managed under the RAPID protocol compared to those who were not[11] as well as durable viral suppression.[12] Similar studies of rapid ART initiation in the United States have shown improved linkage to care and viral suppression seen at a federally qualified health center (FQHC), a large health care system in an urban setting, and a private Infectious Diseases practice.[13-15] International studies have shown improved uptake of ART, retention in care, and virologic suppression with same-day start for ART.[16-18] Furthermore, a recent meta-analysis showed improved patient outcomes in retention in care and viral suppression, with a trend toward improvement in mortality with rapid initiation of ART.[19]

As more data are reported, there is increasing evidence that rapid initiation of ART should be recognized as a practice that improves clinical outcomes and may possibly decrease forward transmission events.[10-24] The World Health Organization and International AIDS Society have guidelines in support of rapid initiation of ART when clinically appropriate.[25,26] However, the rapid initiation protocols from US-based studies have so far involved significant utilization of health care resources in the form of dedicated staff/personnel to assist with patient navigation, linkage, prescribing ART, and sometimes case management services.[11,13,15,22] The purpose of the current study is to evaluate outcomes of individuals diagnosed with AHI in the setting of a routine linkage to care program in Chicago, the Expanded Testing and Linkage to Care (X-TLC) program. We report on the feasibility of implementing rapid initiation of ART for AHI across diverse health care organizations within an ongoing HIV testing and linkage to care program, primarily utilizing existing staff and resources.

Methods

Setting

The X-TLC program includes 13 health care centers on the South and West sides of Chicago, funded through the Chicago Department of Public Health. The sites include hospitals and their associated emergency departments as well as clinics and FQHCs. In total, X-TLC conducted HIV tests on 173 378 persons in 2016 and 2017, and diagnosed 408 new HIV infections. Though similar, each site had its own protocol for screening, result notification, and linkage to HIV care. Six of these sites identified at least 1 AHI and were included in the current report. All sites used a fourth or fifth generation HIV testing platform. Most had an on-site linkage to care staff member or patient navigator, with the exception of one FQHC (site A) where the provider was responsible for initial attempts at linkage. If sites were unable to contact an HIV-positive patient after 3 phone call attempts and a letter, they contacted Chicago Department of Public Health (CDPH). Other methods to reach patients included text messages, email, or a home visit.

Linkage to Care and Initiation of ART

Each site independently decided to implement rapid initiation procedures or to continue existing procedures for linkage of patients. Four of the 6 sites (sites B, D, E, and F; Supplemental Appendix A) reported adopting procedures that supported rapid ART initiation, either specific to AHI or for all new diagnoses. Sites B and D used real-time laboratory results to notify patients and offer patient navigation at the point of care, while X-TLC program staff at sites E and F received HIV test results daily. Sites B, D, E, and F each had a designated infectious diseases (ID) provider who reviewed results on a near-daily basis to expedite linkage to care and determine need for rapid initiation of ART, sometimes starting ART before linkage. Sites B and E aimed to start ART within 72 hours of confirmed diagnosis (confirmed with HIV RNA viral load). Site D was enrolling in a research study for AHI, with a protocol that placed individuals with likely AHI on treatment within 7 days of the initial positive HIV antigen/antibody test. An ID provider at site D assessed each result to determine likelihood of true positive versus false positive based on the signal to cutoff ratio prior to starting ART if awaiting the HIV RNA result. Site F

had accelerated linkage to care for patients with AHI within 7 days of diagnosis. Sites A and C used standard linkage procedures, aiming to link patients to care within 30 days, with no specific timeline for initiation of ART. Linkage staff for site A received laboratory reports daily, while site C received laboratory reports monthly. Initial ART regimen was decided by providers at each site. Resources differed across sites, with sites B, D, E, and F having 2 dedicated linkage navigators and sites A and C with 1 dedicated linkage navigator. Site D had additional research funds, which covered ART for participants and supported clinical trial staff for enrollment after initial linkage was completed. The remaining sites did not have additional funds provided for rapid initiation of ART for treatment of AHI.

Data Collection and Analysis

A retrospective analysis was performed using data collected on all AHIs diagnosed through the X-TLC program from 2016 to 2017. Acute HIV infection was defined as a reactive fourth or fifth generation HIV test (if fifth generation, then reactive p24 antigen and nonreactive Ab), a negative HIV-1/HIV-2 antibody differentiation assay, and a positive HIV RNA viral load. New cases were defined as those that were not previously identified by CDPH or known to the diagnosed individual.

We collected demographic information and CDC HIV transmission category for acute and new HIV infections. For AHI, we examined care continuum outcomes including linkage to care, initiation of ART, 2-log reduction in viral load, viral suppression, and retention in care to date. Linkage to care was defined as attending at least 1 HIV care appointment with an ID specialist or primary care provider. Viral suppression was defined as an HIV RNA viral load less than 200 copies/mL. Retention in care was defined as continued engagement in HIV care from HIV diagnosis until the end of data collection, determined by laboratory tests or a clinical visit within the prior 3 to 6 months. We also documented baseline clinical measurements (HIV viral load and CD4 T-cell count), clinical signs and symptoms associated with AHI, and initial ART regimen. Descriptive statistical analyses were performed using SAS version 9.4. Frequencies and percentages, as well as medians and interquartile ranges (IQR), are reported. We compared baseline characteristics of AHI to other new infections using χ^2 and Kruskal-Wallis median tests.

Ethical Approval and Informed Consent

This study was determined to be IRB-exempt by the Institutional Review Board at The University of Chicago. All individuals provided written consent for general medical care and HIV testing per each institution's policies.

Results

Of 334 new HIV diagnoses across 6 X-TLC sites during 2016 to 2017, 33 (9.9%, range 4.5%-17.5% by site) were AHIs. Most cases were diagnosed at acute care hospitals or emergency departments (EDs; n = 32, 97.0%), although 1 case occurred at an FQHC. Individuals with AHI were mostly young (median age 24 years [IQR: 20-30]), African American (75.8%), and identified as male (90.9%). The primary transmission category was men who have sex with men (n = 25, 75.8%). One patient with AHI was asymptomatic while the remainder presented with symptoms, most commonly fever or gastrointestinal (diarrhea, nausea, or vomiting) symptoms (Table 1). Median viral load measurement at baseline was 2.19 million (6.34 $\log_{10}$) copies/mL (IQR: 0.47-5.00), and median baseline CD4 count was 440.5/μL (IQR: 287.5-568.5; Table 1). Table 1 compares patients with AHI to those with a new diagnosis. Patients with AHI were significantly younger than those with other new diagnoses (24 versus 32 years, $P = .0027$), with higher median baseline viral load (2.19 million versus 49 972 copies/mL, $P < .001$) and higher baseline CD4 count (440.5 versus 277/μL, $P = .0027$).

The median time to linkage was 11 days (IQR: 5-19.5) and median time to ART prescription was 15 days (IQR: 5-27; Table 2). Antiretroviral therapy was confirmed to have been initiated in 31 (93.9%) of patients, with initial ART regimen in Table 1. For care continuum, outcomes related to viral load reduction, the median time to a 2-log reduction in viral load was 58.5 days (IQR: 42-117) and median time to viral suppression was 131 days (IQR: 54-188; Table 2). Overall, 69.7% of patients were retained in care. Of the 10 patients not known to be retained in care, 5 had transferred care outside of the X-TLC network and thus we were unable to determine current retention status, 3 were lost to follow-up and unreachable by the clinical site and CDPH, and 2 had unknown reason for not being retained in care. Patients were followed for a median of 256 days (IQR: 190.5-599) from diagnosis at the time of data collection. Of those retained in care at an X-TLC site (n = 23), 100% achieved viral suppression (Table 2).

Discussion

Acute HIV infections have become increasingly important for HIV testing and care programs. Mounting evidence supports rapid initiation of ART to improve patient outcomes such as viral suppression and the public health outcome of decreased transmission.[19] We evaluated program processes and clinical outcomes for patients diagnosed with AHI in a routine health care-based HIV testing program across multiple health care organizations in Chicago. We found that despite variation across sites within the X-TLC program, clinical outcomes were achieved at similar proportions as those reported in rapid ART projects, primarily using existing program resources.

Comparison to Other Studies

Our patients with AHI presented with symptoms similar to those reported in the literature. However, when comparing to the AHI cohort described by Lin et al, we had a lower rate of asymptomatic patients (3% versus 15%) and myalgias (36.4%

Table 1. Demographic and Baseline Clinical Factors Among Persons With Acute and New HIV Infection in the Expanded Testing and Linkage to Care (X-TLC) Program.

Demographic factors	Acute (N = 33) frequency (%) or median (IQR)	New (N = 301) frequency (%) or median (IQR)	*P* value[a]
Age (years)	24 (20-30)	32 (25-46)	.0027
Sex			.0812
Male	30 (90.9)	207 (68.8)	
Female	3 (9.1)	75 (24.9)	
Transgender male to female	0 (0.0)	1 (0.03)	
Unknown	0 (0.0)	18 (6.0)	
Race			.7302
African American	25 (75.8)	223 (74.1)	
Unknown/other	5 (15.2)	56 (18.6)	
White	3 (9.1)	22 (7.3)	
Transmission category			<.0001
MSM	25 (75.8)	84 (29.8)	
Heterosexual	7 (21.2)	85 (30.1)	
Unknown/other	1 (3.0)	10 (3.6)	
IDU	0 (0.0)	103 (36.5)	
Baseline clinical factors	**Median (IQR)**	**Median (IQR)**	***P* value[a]**
Viral load (copies/mL)	2.19 million (0.5-5.0); 6.34 $\log_{10}$	49972[b] (13167, 134544); 4.67 $\log_{10}$	<.0001
CD4 count (/μL)	440.5 (287.5-568.5)	277[c] (139-475)	.0027
Presenting symptoms			
Fever	22 (66.7)		
Gastrointestinal	22 (66.7)		
Myalgia	12 (36.4)		
Pharyngitis	7 (21.2)		
Rash	1 (3.0)		
No symptoms	1 (3.0)		
Initial ART			
2 NRTIs + INSTI	20 (60.6)		
2 NRTIs + INSTI + bPI	10 (30.3)		
Unknown	1 (3.0)		

Abbreviation: ART, antiretroviral therapy; bPI, boosted protease inhibitor; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; MSM, men who have sex with men; NRTI, nucleoside reverse transcriptase inhibitor.
[a]Chi-squared or Kruskal-Wallis median test.
[b]N = 181.
[c]N = 165.

Table 2. Care Continuum Outcomes Among Persons With Acute HIV Infection at 6 Health Care Sites in the Expanded Testing and Linkage to Care (X-TLC) Program.

Site (new HIV infections)	AHI (%[a])	Median days to linkage (IQR)	Received ART (%)	Median days to ART (IQR)	Median days to ≥ 2 log reduction (IQR)	Median days to VL ≤ 200 (IQR)	VS ever (%)	Retained in care[b] (%)	VS at end of follow-up (%[c])
A (22)	1 (4.5)	27 (27-27)	1 (100.0)	9 (9-9)	55 (55-55)	55 (55-55)	1 (100.0)	1 (100.0)	1 (100.0)
B (80)	6 (7.5)	11 (6-58)	6 (100.0)	21.5 (7-58)	48 (34-62)	132.5 (48-321)	4 (66.7)	4 (66.7)	4 (100.0)
C (29)	2 (7.1)	39 (39-39)	1 (50.0)	53 (53-53)	95 (95-95)	162 (162-162)	1 (50.0)	1 (50.0)	1 (100.0)
D (36)	4 (11.1)	3.5 (1.5-4.5)	3 (75.0)	4 (3-6)	31 (29-33)	31 (29-33)	3 (75.0)	3 (75.0)	3 (100.0)
E (80)	14 (17.5)	8.5 (4-18)	14 (100.0)	5.5 (4-21)	55 (47-131)	124 (55-162)	14 (100.0)	10 (71.4)	10 (100.0)
F (87)	6 (6.9)	14 (13-21)	6 (100.0)	25.5 (23-34)	92.5 (62-471)	329.5 (186-643)	6 (100.0)	4 (66.7)	4 (100.0)
Total (334)	33 (9.9)	11 (5-19.5)	31 (93.9)	15 (5-27)	58.5 (42-117)	131 (54-188)	29 (87.9)	23 (69.7)	23 (100.0)

Abbreviations: AHI, acute HIV infection; ART, antiretroviral therapy; IQR, interquartile range; VL, viral load; VS, viral suppression.
[a]Acute HIV infection as percentage of new HIV infections, by site.
[b]Retained in care at one of the X-TLC sites.
[c]Viral suppression as percentage of those retained in care at one of the X-TLC sites.

versus 52.2%) and higher percentage of patients with fever (66.7% versus 60.2%) and gastrointestinal symptoms (66.7% versus 37.2%) when looking at symptoms in the 14 days prior to testing.[27] The number of AHI identified in the current study was comparable to that seen in some studies of rapid ART initiation and higher than seen in others (see Supplemental Appendix B for comparison table).[11,21]

Direct comparison of care continuum outcomes seen in our study to those previously published in other studies is difficult due to differences in patient composition, intervention, and outcome measures. For instance, we measured time to ART and viral suppression from date of diagnosis, while others measured these outcomes from linkage to care.[15] As expected for an observational study, our time to milestones on the care continuum took longer than that seen in other studies explicitly designed to be rapid ART interventions. In our patients with AHI, it took a median of 15 days from diagnosis to receive an ART prescription, and a median of 131 days to achieve viral suppression from a baseline median viral load of 6.34 $\log_{10}$ copies/mL. This is longer than that reported by other rapid ART interventions, for 2 reasons. Firstly, almost all studies of rapid ART did not include sizable numbers of AHI, reducing the baseline median viral load and shortening the time to viral suppression.[11,13,15] In our patients, a median viral load of 6.34 $\log_{10}$ copies/mL suggests these patients were presenting near the time of peak viral load and was higher than the viral load seen in other studies. Secondly, for interventions designed to promote rapid ART, specific resources were devoted to achieve clinical outcomes.[11-13,15,21]

Our retention in care rate was 69.7%, which includes patients who transferred care to another clinic site or who had moved out of Chicago to a different jurisdiction. One other study provided enough information to calculate retention in care for those that both transferred care and those that were lost to follow-up, and our proportion retained in care is similar to both that study and an additional study that had a follow-up period of longer than 6 months.[11,21] For those patients for whom we had subsequent follow-up data, there was durable viral suppression at a proportion as good as that seen in other studies (Supplemental Appendix B).[11-13,15,21]

Implications for implementation of rapid ART initiation. Time to ART initiation and time to viral suppression varied widely among the 6 X-TLC sites included in the analysis. The variation in clinical outcomes likely reflects the lack of a unified protocol for management of AHI across sites, with some sites focusing on linkage to care within a short time period with initiation of ART at the discretion of the provider, while other sites specifically aimed to rapidly initiate ART (Supplemental Appendix A). This variation in protocols provided an opportunity to identify processes that result in the desired patient outcomes and allowed us to demonstrate that rapid ART initiation can occur in a diversity of settings. An important difference between the current study and others reported in the literature is the amount of dedicated resources devoted to rapid initiation of ART. Nearly all sites within X-TLC (with the exception of site D) utilized existing staff and operating procedures to manage initiation of ART for AHI. However, site D, which had clinical trial staff and funding dedicated to this purpose, demonstrated the fastest linkage to care, initiation of ART, and viral suppression of all the X-TLC sites. By sharing of protocols among sites in the X-TLC program, sites have been able to further modify their local practices, which may enhance rapid initiation efforts without requiring additional resources.

In reviewing processes that enabled rapid initiation of ART across organizations, we were able to identify some key similarities. Routine HIV screening was already in place and sites had established procedures for notification and linkage to care. This was assisted by timely reporting of laboratory results. Some sites received results in real-time, and most were able to confirm positive diagnoses on a daily basis. Sites also had experience in addressing barriers to linkage to care that would preclude rapid initiation of ART, that is, patient transportation needs, insurance issues related to payment for labs and clinic visits, and assistance in obtaining ART and ART drug coverage. Finally, most sites had experienced HIV care providers, which greatly expedited linkage and rapid initiation. Having a network of participating health care facilities to accommodate referrals depending on insurance coverage and patient preference helped with this process.

Although demonstration projects have established the feasibility and improved individual patient outcomes of rapid ART initiation, it is difficult to measure the downstream effects of rapid ART for AHI on the HIV epidemic overall. There has been discussion that despite high viral loads, the relatively short time spent in acute and early HIV stages may result in a limited role in population HIV transmission.[28,29] There is also evidence that incident cases decrease following AHI diagnosis without ART initiation, suggesting that knowing your HIV status is also a factor in reducing forward transmission.[30] Further research is needed to help us understand how quickly patients must enter care in order to demonstrate the benefits in retention and viral suppression while still using health care resources parsimoniously.

Limitations

There are several limitations to this study. First, it is a retrospective descriptive analysis. We were unable to examine earlier cases since fourth-generation HIV testing has only recently allowed for consistent detection of AHI. While most X-TLC sites did not have additional funding to implement rapid initiation of ART, program funds did provide support for linkage to care and patient navigation; rapid initiation of ART took additional time from program staff for counseling, education, navigation of pharmacy benefits, and so on, that may otherwise not occur until time of linkage to care. In addition, we do not know clinical outcomes for patients referred to care outside of the X-TLC sites. While we try to keep patients in the X-TLC network, location of care is sometimes decided by insurance coverage and patient choice. While screening and linkage programs may serve as a method to scale up rapid initiation or

ART, routine HIV screening itself faces barriers to implementation that could limit this approach.[31,32] We primarily examined outcomes for AHI; some of the X-TLC sites also provided rapid ART for all patients newly diagnosed with HIV. Including these data may provide additional insight into feasibility and consistency in clinical outcomes. Finally, since each X-TLC site is responsible for developing their own procedures for management of AHI and rapid initiation of ART, we did not have a uniform intervention that can be used as a template for future studies to emulate. However, we did identify some key components that are likely to contribute to successful implementation of rapid initiation of ART across diverse clinical settings.

Conclusions

Our data demonstrate that management of patients with AHI can be successfully incorporated into existing programs for HIV screening and linkage to care. The X-TLC program had a high linkage to care rate, timely initiation of ART, and rapid reduction in viral loads for AHI. Our outcomes approach those seen in US-based studies, with few additional costs and resources required. This suggests that it is feasible to scale up this intervention to health care organizations with existing HIV testing programs. Increasing routine health care–based HIV screening in high prevalence areas using fourth-generation HIV tests, particularly in EDs, may facilitate increased diagnosis of AHI. Future work should be directed to better understanding if efforts for rapid initiation of ART actually decrease new HIV transmission events, potentially by interrupting transmission chains and reducing community viral load. Incorporating rapid initiation of ART into existing programs for routine HIV screening and linkage to care may provide a cost-effective method of scaling up this important intervention and deserves more investigation.

Declaration of Conflicting Interests

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