Asymptomatic Adolescent HIV: Identifying a Role for Universal HIV Screening in the Pediatric Emergency Department

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Abstract

Adolescents account for most undiagnosed HIV infections in the United States. Although the Centers for Disease Control and Prevention (CDC) recommends universal HIV screening for all patients ≥ 13 years, <10%of adolescents have been tested for HIV. To identify earlier opportunities for adolescent HIV prevention and diagnosis in a region of high HIV prevalence, we sought to describe pediatric emergency department (PED) visits made by a retrospective cohort of adolescents who were later diagnosed with HIV as young adults (<25 years) through an adult emergency department (ED) universal HIV screening program. CD4+ count was used to estimate the time of HIV infection before diagnosis and all PED visits in the 10 years before diagnosis were analyzed. Universal HIV screening in the adult ED diagnosed 193 young adults (median 22 years; 90%) men; 29% stage 3); 70% had CD4+ at diagnosis that was used to estimate time of infection (mean 3.8 years). Thirty-eight HIV-infected young adults had a total of 109 PED visits in the 10 years before HIV diagnosis. Sexual history was documented in 12% of PED visits and a sexually transmitted infection test was sent in 6%. Ten HIV-infected young adults had 26 PED visits during the time in which they were likely already infected with HIV, each a potential missed opportunity for earlier diagnosis. HIV-infected and at-risk adolescents are underrecognized in PED visits. Implementation of CDC-recommended universal screening may lead to earlier diagnoses and improve outcomes; the PED may also be critical in identifying adolescents eligible for preexposure prophylaxis.

Keywords: HIV, adolescent, emergency department, screening

Introduction

IN THE UNITED States, there is an ongoing epidemic of HIV with striking disparities across the country. Adolescents and young adults 13–24 years comprise 20% of new diagnoses of HIV¹ and are the age group that is most likely to be unaware of their diagnosis.^{2,3} The South is disproportionately affected by the HIV epidemic; the Atlanta Metropolitan Statistical Area has the second highest rate of new HIV diagnosis in the United States,⁴ and adolescents and young adults in this region are at high risk for late HIV diagnosis.^{5–9} Early diagnosis of HIV is essential as it allows prompt initiation of antiretroviral therapy, arresting disease

progression, and promoting immunologic recovery,^{10–12} while reducing disease transmission.^{13–18} As such, the Centers for Disease Control and Prevention (CDC) recommend that all individuals 13–64 years receive routine HIV screening.¹⁹ Despite these recommendations, adolescents are uncommonly tested for HIV and pediatric providers have low knowledge of HIV screening recommendations and infrequent HIV testing practices.^{20–23}

The emergency department (ED) has been established as a critical location for HIV screening, and CDC-recommended universal HIV screening has been successfully implemented in general EDs across the United States.^{24–28} There are also efforts to identify ED patients at high risk for HIV to facilitate

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referrals for preexposure prophylaxis (PrEP) initiation.²⁹ The ED may be particularly important in HIV prevention and diagnosis in adolescents, who often seek care in the ED instead of primary care clinics.^{30,31} However, adolescents are infrequently assessed for HIV risk or tested for HIV in the pediatric emergency department (PED).³²⁻³⁴ Adolescents who are unaware of their infection may pass undetected through the PED and subsequently present as young adults with late-stage HIV in adult health care settings. To understand the potential missed opportunities for adolescent HIV prevention and diagnosis, this retrospective study of young adults diagnosed with HIV through adult ED universal screening in a region of high HIV prevalence seeks to (1) describe the PED visits made by those young adults in the 10 years preceding HIV diagnosis and (2) identify those PED visits that occurred when the adolescent was likely already infected with HIV.

Methods

Study design, setting, and participants

This is a retrospective cohort study of young adults diagnosed with HIV through adult ED universal screening between 2013 and 2017. Serum-based opt-out HIV screening took place in the ED of Grady Health System, a large academic safety-net hospital and Level 1 trauma center with >120,000 annual ED patient visits in Atlanta, GA, an urban area with high HIV prevalence.⁸ Patients were included if they were evaluated in this ED between January 1, 2013 and December 31, 2017, were <25 years old at the time of evaluation and had a positive HIV screening test (HIV antibody or HIV antibody/antigen) during their ED visit. Patients were excluded if they had negative or indeterminate HIV testing³⁵ or if they were identified as having a previous HIV diagnosis and had previously established HIV care. PED visits took place in any of the three PEDs at Children's Healthcare of Atlanta, a children's hospital network in the same metropolitan area with 34 pediatric HIV diagnoses between 2013 and 2017;⁶ each PED is part of a free-standing children's hospital with >240,000 combined annual ED patient visits. This study was approved by the Children's Healthcare of Atlanta Institutional Review Board and by the Grady Health System Research Oversight Committee.

Data collection and analysis

From each adult ED visit, data collected included patient demographics (age, sex, year of ED visit) and HIV testing results (screening test result, viral load, CD4+ count). HIV stage at diagnosis was defined by CD4+ count³⁵ at the time of

diagnosis. Charts were manually reviewed to identify patients meeting exclusion criteria.

PED charts were reviewed to identify all PED visits that had occurred for each patient in the 10 years preceding the positive HIV test. Data collected from PED charts included patient and ED visit characteristics (age at time of PED visit, year of PED visit, and chief complaint). Chief complaint was categorized as related to an injury, abdominal pain, asthma, genitourinary or gynecologic (GU/GYN) symptoms, nonspecific infectious symptoms (such as fever, cough, cold, and sore throat) that were not GU/GYN, behavioral concern, or mental health symptoms, or other. Each visit was reviewed to determine if a sexual history was documented by the provider and if any testing for pregnancy and/or sexually transmitted infections (STIs, including gonorrhea, chlamydia, trichomonas, syphilis, and HIV) was obtained. Descriptive statistics, including median, interquartile ranges, mean, and standard deviations, were used to analyze the data.

The CD4+ at the time of HIV diagnosis was used to determine a conservative estimate of the time period for which the patient had been infected with HIV before the diagnosis.^{2,36–38} Only patients with an available CD4+ count were included in the analysis of estimated time of infection. A CD4+ of 500 cells/ μ L was determined to be the lower limit of normal and patients with a CD4+ of 500 cells/ μ L or greater were assumed to have been infected with HIV for 1 year or less. Thereafter, it was assumed that each year of HIV infection was associated with a decline of CD4+ by 60 cells/ μ L per year. This conservative model was previously published and consistent with estimated times from seroconversion to CD4+ count from large populations of untreated HIVinfected individuals, which demonstrate that the time to CD4+ <350 cells/ μ L and CD4+ <200 cells/ μ L may in fact be even longer than that predicted by this model.^{2,36,38–40}

Results

Between 2013 and 2017, 228 young adults met initial inclusion criteria; 22 patients were subsequently determined to have negative or indeterminate test results and were excluded and an additional 13 patients were excluded on chart review as they were known to have HIV and had previously established HIV care. A total of 193 patients were included in the remaining data collection and analysis (Fig. 1). The median age at diagnosis was 22 years (interquartile range = 20–23 years). A total of 133 patients were CD4+ at diagnosis and were included in the analysis of estimated time of infection. For these 133 patients, the median CD4+ at diagnosis was 311 (interquartile range = 177–459), with median time of infection of 5 years (interquartile range = 2–7 years) before



FIG. 1. Flow diagram of young adults included in cohort. PED, pediatric emergency department.

diagnosis. Twenty percent of the cohort had Stage 3 HIV based on CD4+ at the time of diagnosis. Additional patient characteristics are given in Table 1.

Thirty-eight patients (20%) had been seen in the PED at least once in 10 years before HIV diagnosis, for a total of 109 PED visits. The median time between most recent PED visit and HIV diagnosis was 5 years (interquartile range=3-7 years). The median number of PED visits per patient was 2.5 (interquartile range=2-3 visits). The most common reason for PED visit was for evaluation of an injury or nonspecific infectious symptoms (such as fever, cough, cold, and sore throat). Sexual history was documented in 12% of visits representing seven patients and STI testing was obtained in 6% of visits representing four patients. Table 2 provides additional characteristics of the PED visits that occurred in the 10 years before HIV diagnosis.

Ten patients were seen in the PED during the timeframe in which they were likely infected with HIV. These 10 patients had 30 total PED visits in the 10 years before HIV diagnosis, 26 of which occurred in the period in which the adolescent was likely infected with HIV (Table 3). The mean time between the most recent PED visit while presumed to already be infected and the HIV diagnosis was 3.8 years. Sexual history was documented for five of these patients over seven visits in which they were presumed to be HIV infected and STI testing was sent in two of these visits for two separate patients. This included one test for HIV, which was positive; this 17-year-old patient was called back to the PED for diagnosis disclosure and referred to HIV outpatient care. This patient was subsequently lost to follow-up until testing positive for HIV through adult ED based opt-out screening 2 years later, at which time this patient was admitted to the hospital with Pneumocystis *jirovecci* pneumonia and CD4+ count of 16 cells/ μ L.

 TABLE 1. PATIENT CHARACTERISTICS AT TIME OF POSITIVE HIV SCREEN

| | <i>All</i> (n=193) | No prior PED visit (n=155) | Prior PED visit (n=38) |
|-------------------|--------------------|----------------------------------|------------------------------|
| Sex, n (%) | | | |
| Male | 172 (89) | 141 (91) | 31 (82) |
| Female | 19 (10) | 12 (8) | 7 (18) |
| Transgender | 2 (1) | 2 (1) | 0 |
| Age | | | |
| Mean ± SD | 21.8 ± 1.8 | 22.0 ± 1.8 | 20.9 ± 1.7 |
| Median | 22.0 | 22.0 | 21.0 |
| Range | 16–24 | 16–24 | 18-24 |
| Year, n (%) | | | |
| 2013 | 14 (7) | 13 (8) | 1 (3) |
| 2014 | 39 (20) | 30 (19) | 9 (24) |
| 2015 | 46 (24) | 41 (27) | 5 (13) |
| 2016 | 49 (26) | 37 (24) | 12 (31) |
| 2017 | 45 (23) | 34 (22) | 11 (29) |
| CD4+, n (%) | | | |
| >500 (Stage 1) | 26 (14) | 22 (14) | 4 (11) |
| 200-499 (Stage 2) | 68 (35) | 52 (34) | 16 (42) |
| <200 (Stage 3) | 38 (20) | 30 (19) | 8 (21) |
| Not available | 60 (31) | 50 (33) | 10 (26) |

PED, pediatric emergency department; SD, standard deviation.

 TABLE 2. CHARACTERISTICS OF PEDIATRIC EMERGENCY

 DEPARTMENT (PED) VISITS

| | N = 109 PED visits |
|---|--------------------|
| Age at PED visit, years | |
| Mean±SD | 15 ± 1.9 |
| Median | 15 |
| Range | 9–18 |
| Chief complaint, n (%) | |
| Injury | 24 (22) |
| Infectious symptoms | 20 (18) |
| Asthma | 8 (7) |
| GU/GYN | 4 (4) |
| Abdominal pain | 4 (4) |
| Behavioral Complaint | 3 (3) |
| Other | 46 (42) |
| Sexual history documented, n (%) | |
| Yes | 13 (12) |
| No | 96 (88) |
| Pregnancy test sent. ^a n (%) | |
| Yes | 8 (31) |
| No | 18 (69) |
| Any STI testing $b n (\%)$ | |
| Yes | 6 (6) |
| No | 103 (94) |
| | (-) |

 $^{a}n = 26$ PED visits for seven female patients.

^bSTI testing includes testing for gonorrhea/chlamydia (five visits), trichomonas (two visits), syphilis (two visits), HIV (two visits), hepatitis B (one visit).

GU/GYN, genitourinary or gynecologic; PED, pediatric emergency department; SD, standard deviation; STI, sexually transmitted infection.

Discussion

In this retrospective cohort of young adults diagnosed with HIV through ED-based universal screening, previous PED visits during adolescence were common. During those visits, the majority of these adolescents were not assessed for HIV risk and did not receive HIV testing; at least 10 individuals (5.2% of the total cohort) were likely already infected with HIV when visiting the PED. In all, the numerous PED visits made by these HIV-infected adolescents represent missed opportunities for prevention and earlier diagnosis of HIV.

In 2019, the US Department of Health and Human Services proposed "Ending the HIV Epidemic: A Plan for America."⁴¹ This initiative focuses efforts on diagnosis, treatment, and prevention in regions of highest HIV prevalence. Our data identified a population of young adults in a high-prevalence region who were diagnosed with late-stage HIV and who may have benefitted as adolescents from prevention efforts and earlier diagnosis in the PED. Although the total number of PED visits made by patients in our cohort represents only a small fraction of the visits made in our system, each of the 109 visits made by these patients was a missed opportunity to substantially impact individual and public health.

Sexual health risk factors for HIV were unlikely to be documented by PED providers in this cohort of individuals diagnosed with HIV as young adults. Gathering a complete sexual history on each adolescent patient may be perceived as difficult in a busy ED. Adolescents in our cohort infrequently presented for specific GU or GYN concerns that might otherwise alert the provider to collect a sexual history. Testing

| Age ^a (years), sex | CD4+ ^a | PED visits ^b | Chief complaint ^c | Sexual history documentation ^c | STI testing ^c |
|----------------------------------|-------------------|-------------------------|--|--|---|
| 21, M | 3 | 7 | Injury (two); asthma (two); behavioral concern (two: SI); other (two: nipple discharge; syncope) | None | None |
| 20, M | 344 | 4 | Other (four: seizure) | None | None |
| 19, M | 16 | 3 | Asthma (four); infectious symptoms (one); other (one: call back for positive HIV) | "Sex with women, occasional condom use" | RPR negative, HIV positive ^d |
| 21, M | 3 | 3 | Abdominal pain (one); other (two: chest pain and fatigue; rectal pain) | "Last female sex 2 weeks, 100% condoms, 5–6 partners"; "Sexually active, uses condoms" | None |
| 20, M | 172 | 2 | GU/GYN concern (one: request for STI test); other (one: bump on ear) | "Male partner" | GC/CT negative, <i>Trichomonas</i> negative |
| 21. M | 233 | 2 | Iniury (two) | None | None |
| 20, F | 278 | 2 | Other (one: vomiting); infectious symptoms | "Sexually active, uses protection"; "Sexually active, uses protection often but not always" | None ^e |
| 20, M | 11 | 1 | Other (one: headache) | None | None |
| 20, M | 26 | 1 | Behavioral concern (one: suicidal ideation) | None | None |
| 18, F | 180 | 1 | Injury | None | None |

TABLE 3. PATIENTS WITH PEDIATRIC EMERGENCY DEPARTMENT VISITS WHILE PRESUMED TO BE INFECTED WITH HIV

^aAt time of HIV diagnosis.

^bWhile presumed to be infected with HIV.

^cAt PED visit(s).

^dReferred for outpatient care and lost to follow-up.

^eNegative pregnancy testing.

F, female; GC/CT, gonorrhea and chlamydia testing; M, male; PED, pediatric emergency department; RPR, rapid plasma reagin (syphilis screening); STI, sexually transmitted infection.

for STIs was also low, which may reflect competing priorities in clinical care or physician knowledge gaps. Consistent with other studies in finding suboptimal HIV testing practices during adolescent STI evaluations,^{23,32} a high-risk adolescent who requested STI testing was not tested for HIV at an ED visit in which he was likely already infected with HIV (Table 3). Adolescents with high-risk sexual behaviors are more likely to seek care in the ED than with a primary care provider,⁴² and the ED setting represents a critical point of contact with this vulnerable population. There are a few clear opportunities for improvement that may maximize the ability to best support these adolescents.

First, universal adolescent HIV screening in the PED, as recommended by the CDC, may be critical in identifying early infection in asymptomatic adolescents. There are few existing PED universal HIV screening programs,43-47 reflecting the unique needs to consider in implementing such a program in adolescents. However, late diagnosis of HIV was common in our cohort of young adults, highlighting the role of pediatric providers in diagnosing adolescent HIV before it progresses to late-stage disease in early adulthood. Ten patients in our cohort had 26 PED visits during which their HIV infection was potentially missed. In most cases, the chief complaint did not obviously indicate a need for HIV testing. In retrospect, in four instances the adolescent presented with vomiting, headache, or other acute infectious symptoms; this presentation is common and nonspecific, but it is possible that the adolescents were experiencing the nonspecific symptoms of acute HIV infection. In contrast to targeted screening, which relies on provider identification of risk factors, universal HIV screening eliminates the need for risk factor identification and disclosure. This mitigates provider knowledge gaps^{21,22} and bias³² and simultaneously normalizes HIV screening, which may reduce societal stigma and HIV health disparities.⁴⁸

In addition to universal HIV screening, there may additionally be opportunities for HIV prevention in the adolescent PED visit. PrEP has recently been approved for HIV prevention in adolescents and has high acceptability among adolescents and their parents.⁴⁹ Many of the adolescents in our cohort had PED visits before they were infected with HIV; identifying such adolescents for referral for PrEP initiation may be a critical opportunity to decrease transmission in this population. There are existing models for public health interventions in adolescents in the ED^{50-52} and adolescents, parents, and ED administrators are receptive to sexual health interventions in this setting.^{31,53–55} Computerized surveys have been used to identify adolescents in the PED with psychiatric and sexual health needs while minimizing impact on clinician workflow and length of stay.^{56–59} Similar efforts may support HIV prevention; future work is needed to explore ways of identifying eligibility for PrEP initiation and referral in adolescent PED patients while maintaining patient confidentiality and ED flow.

This study is subject to limitations. This was a retrospective study that was conducted at two distinct centers and is subject to limitations inherent to this study design. The results may not be generalizable to other institutions, particularly in

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areas in which HIV prevalence is low. Identifying patients who met exclusion criteria owing to previous HIV diagnosis and had previously accessed HIV care was sometimes reliant on provider documentation of patient self-report, if the patient's HIV care was obtained outside our institution. Although there is individual variability in CD4+ response to HIV infection and we cannot confirm the period in which each individual was infected with HIV before diagnosis, we selected a conservative model for this analysis to minimize the chance of overestimation of the period of infection. The finding of one positive HIV test in the PED in an individual predicted to be HIV infected is supportive of the accuracy of our analysis. Furthermore, the rate of decline in CD4+ is inversely associated with age,^{60,61} and so our adolescent population may in fact have been infected for even longer than predicted by our model. All the patients that we identified as having at least one PED visit during the estimated time in which they were already infected with HIV had CD4+ $<350 \text{ cells}/\mu\text{L}$, and eight had CD4+ $<200 \text{ cells}/\mu\text{L}$. Because of the conservative nature of this model, it is possible that there were even more patients from our cohort who were seen in the PED while HIV infected than we identified.

In this region of high HIV prevalence, young adults diagnosed with HIV through ED-based opt-out screening often presented with late-stage HIV. These individuals may have benefitted from earlier diagnosis or prevention efforts in adolescence. Many had previously been seen in the PED, where sexual history was infrequently documented and HIV testing was rare. A subset of patients was seen in the PED when they were likely already infected with HIV, representing missed opportunities for early diagnosis. Adolescents with asymptomatic HIV will likely go unrecognized in PED visits. Implementation of CDC recommended universal HIV screening in the PED in high-prevalence areas may increase early HIV diagnosis, reduce health disparities, and has the potential to save lives. Our findings support future work to develop PrEP eligibility assessments and implementation processes for universal HIV screening in adolescents presenting to the PED.

Author Contributions

C.K.G. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. C.K.G. participated in study conceptualization and design, acquisition and analysis of the data, drafting of the article, and critical revision of the article. L.M., A.C.-G., and C.R.M. participated in study conceptualization and design and critical revision of the article. Z.B. and B.S. participated in acquisition of the data and critical revision of the article.

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ACG has received funding personally from Theratechnologies Inc. for consulting. CRM is the inventor or co-inventor of several UCSF-Benioff Children's Hospital Oakland patents/ patent-pending applications that include nutritional supplements, and biomarkers of cardiovascular disease, is an inventor of an Emory University School of Medicine patent application for a nutritional supplement, is a consultant for Pfizer, Nestle Nutritional Institute and Calithera Biosciences, Inc, and has received research support from MAST Therapeutics, the United States Food and Drug Administration, and the National Institutes of Health. BS has received salary support for FOCUS HIV screening in the ED from Gilead Sciences, Inc. Grady Health System FOCUS is partially funded by the Gilead Sciences FOCUS program. This program limits its support to testing and linkage to care. FOCUS does not support treatment efforts and remains agnostic to partners' treatment decisions.

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