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Cervical Pap Screening Cytological Abnormalities among HIV-Infected Adolescents in the LEGACY Cohort

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Abstract

Objectives—To determine the prevalence of cervical Pap screening (CPAP-S), identify factors associated with CPAP-S, and explore risk factors for abnormal cervical cytology in female adolescents with perinatally and behaviorally acquired HIV infection.

Design—Cross-sectional

Setting—LEGACY is a national observational cohort chart review study of 1478 HIV-infected persons (age 24 years) managed in 22 HIV specialty clinics in the United States.

Participants—Sexually active females aged 13–24 years in the LEGACY cohort

Main Outcome measures—CPAP-S & abnormal cervical cytology.

Results—Of 231 sexually active female participants (≥ 13 years) in 2006, 49% had CPAP-S documented since 2001. 58% of 113 cervical tests were abnormal (2% high-grade). In multivariable analysis, perinatal HIV infection and black race were associated with decreased likelihood of CPAP-S (adjusted prevalence ratio [APR] 0.66, 95% CI 0.45, 0.96 and APR 0.74, 95% CI 0.56, 0.96, respectively). Presence of any STI was independently associated with increased likelihood of CPAP-S (APR 1.56, 95% CI 1.21, 2.02). CD4⁺ T-lymphocyte count <200 cells/mL and previous STI were independently associated with increased likelihood of abnormal cervical cytology (APR 2.19, 95% CI 1.26, 3.78 & APR 1.94, 95% CI 1.29, 2.92, respectively).

Conclusions—Among sexually active HIV-infected adolescent females, prevalence of CPAP-S was low and cytology was abnormal in more than half of Pap smears. Perinatally HIV-infected, sexually active females were less likely to undergo CPAP-S than their behaviorally HIV-infected counterparts. Interventions targeted at HIV-infected adolescents and care providers are needed to

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improve CPAP-S in HIV-infected young women, especially those with perinatally acquired HIV infection.

Keywords

Cervical Pap screening; HIV infection; Adolescents

Background

Human immunodeficiency virus (HIV) infection in women is associated with an increased risk of human papillomavirus (HPV)-associated malignancies, including cervical cancer¹⁻⁴. The prevalence of cervical neoplasia among HIV-infected women ranges from 11% to 60%, and increases with the degree of immunosuppression⁵⁻⁸. Cervical cytologic abnormalities tend to progress more rapidly to invasive cervical cancer in HIV-infected than in non-infected women⁹.

The Papanicolaou (Pap) test is an effective, low-cost screening test for detecting abnormal cytology or neoplasia in desquamated epithelial cells. Introduction of cervical cancer screening programs using the Pap test has been shown to reduce cervical cancer incidence rates by 60% to 90% within three years of implementation¹⁰. Cervical cancer screening allows early detection, diagnosis, and treatment of cervical cytologic abnormalities before invasive disease appears. In view of the increased risk of cervical cancer in HIV-infected persons, current guidelines issued by the US Public Health Service and the Infectious Diseases Society of America call for more intensive screening for cervical neoplasia in HIV-infected women than in women without HIV infection¹¹⁻¹³. A comprehensive gynecologic examination, including a pelvic examination and cervical Pap test, is recommended as part of initial HIV evaluation. The Pap test should then be repeated at six months and one year after the initial evaluation. If these results are normal, Pap testing may be performed annually thereafter.

Few studies have evaluated adherence to guidelines for cervical Pap screening (CPAP-S) in HIV-infected women, and fewer still have examined adherence to these guidelines in HIV-infected young women. In a national study, during 2000–2004, nearly 1 in 4 (23%) HIV-infected women in the United States did not receive an annual Pap test¹⁴. The actual level of CPAP-S among HIV-infected women is likely lower because ascertainment of Pap testing in this study was based on self-report, which has been shown to overestimate the rate of cervical cancer screening by as much as one-quarter to one-third¹⁵⁻¹⁷.

In a study of socio-demographic, clinical and provider factors associated with screening for cervical cancer in a nationally representative sample of HIV-infected women receiving care in the United States, 81% of eligible women received cervical screening in the past 12 months¹⁸. Women receiving care at clinics with both a gynecologist and primary care physician on site were almost twice as likely as other women to report Pap testing. Twenty-seven percent of Pap tests were abnormal and younger women were more likely than older women to have an abnormal Pap smear result (odds ratio, 5.5; $p < 0.01$) in that study. This finding may be especially relevant to long term surviving perinatally HIV infected adolescents who often receive medical care in pediatric clinics where reproductive health

issues may not be routinely addressed. In the Pediatric AIDS Clinical Trials Group Protocol 219C, only 101 (58.1%) of 174 perinatally HIV-infected female adolescents 13 years and older known to be sexually active had a documented Pap test¹⁹. However, because cervical Pap tests were administered as part of the 219C protocol, this reported CPAP-S rate may be an overestimate. This analysis was restricted to perinatally HIV-infected adolescents, so did not include rates of CPAP-S for adolescents who acquired HIV behaviorally.

The objective of our study was to determine the prevalence of CPAP-S, identify factors associated with CPAP-S, and explore rates of and risk factors for abnormal cervical Pap cytology among HIV-infected female adolescents (13 – 24 years) with perinatally and behaviorally acquired HIV infection participating in the Longitudinal Epidemiologic Study to Gain Insight into HIV/AIDS in Children and Youth (LEGACY) study.

Methods

The study population was drawn from the LEGACY study. LEGACY is a CDC-funded, observational, prospective, cohort study of 1478 HIV-infected children and adolescents between birth and 24 years of age from 22 HIV specialty clinic sites across the US. Clinical LEGACY sites (see appendix) were selected using a 3-stage cluster probability proportional to size sampling method to encourage a broad selection of HIV-infected infants, children and adolescents receiving care in 22 geographically diverse small, intermediate, and large-sized facilities.

LEGACY Study Recruitment

Between November 28, 2005 and June 6, 2007, HIV-infected children and youth presenting for care in LEGACY sites were offered enrollment. Participation was voluntary and written informed consent or parental consent and minor assent were obtained, as appropriate. Participants were not compensated. This study was approved by the Institutional Review Board (IRB) of CDC and the IRBs of all local study sites. A consolidated 301(d) Certificate of Confidentiality was obtained for LEGACY to provide an added level of strict privacy protection for participants. At enrollment, subject medical records were reviewed and abstracted by a data abstractor within one month of each clinic visit of each participant. The last visit by any study participant was on December 18, 2007. Data collected for all study participants included demographics; mode of HIV acquisition; diagnosed conditions (definitive and presumptive); antiretroviral (ARV) and non-ARV medications; vaccinations ; laboratory test results, including CD4+ T-lymphocyte (CD4) cell counts, plasma HIV-RNA determinations, cervical Pap test results; hospitalizations; reproductive history (age at menarche, sexual activity, contraceptive use, history of previous pregnancies, diagnosed sexually transmitted infections (STI) and mortality data. All variables collected prospectively were also collected retrospectively dating back to January 1, 2001.

The primary goal of the present analysis was to determine the prevalence of cervical Pap testing and identify factors associated with cervical Pap testing in sexually active, HIV-infected female adolescents (13 – 24 years old) in this cohort. All females in the LEGACY cohort, at least 13 years old by the end of January 2006, were eligible. Participants who were not documented to be ever sexually active were excluded. Sexual activity was identified

through disclosure to clinic personnel or any record of pregnancy or a STI in the study period. The primary outcome variable was documented cervical Pap testing (ever/never) between 2001 and 2006. Cervical Pap smear results were categorized as normal, abnormal (for any abnormal finding), or unknown/missing (for results which were not recorded or still pending at the end of the study period). The 2001 Bethesda System for reporting cervical cytologic results uses the following classifications: normal, atypical squamous cells (ASC), low-grade squamous intra epithelial lesions (LSIL), high-grade squamous intra-epithelial lesions (HSIL) and squamous cell carcinoma (SCC)²⁰. ASC is subdivided into 2 categories: atypical squamous cells of undetermined significance (ASC-US) and atypical squamous cells, cannot exclude HSIL (ASC-H). Glandular cell abnormalities are similarly classified: atypical glandular cells of undetermined significance (AGC-US) and atypical glandular cells, cannot exclude HSIL (AGC-H). The WHO system on the other hand reports degrees of cervical dysplasia or cervical intraepithelial neoplasia (CIN) - CIN I (mild dysplasia confined to the lower one-third of squamous epithelium), CIN II (moderate dysplasia confined to the lower two-thirds of squamous epithelium), and CIN III (severe dysplasia / carcinoma in situ) that involves from two-thirds to full thickness of squamous epithelium. For this analysis, an abnormal Pap smear was defined as a Pap smear finding of: ASC, ASC-US, ASC-H, AGC-US, AGC-H, LSIL, HSIL, CINI, CINII, CINIII, SCC or glandular cell carcinoma.

Our primary exposure of interest for this analysis was the reported mode of HIV acquisition, categorized as perinatal or behavioral. Participants were considered to have acquired HIV perinatally based on documentation of maternal HIV infection during pregnancy, labor, or delivery and diagnosis of HIV infection in the child during infancy or early childhood (including participants infected via breastfeeding). Persons infected with HIV via consensual sexual activity (CSA), injection drug users [IDU] and persons with more than one risk (CSA, IDU, other) but no perinatal exposure were classified as behaviorally infected. Participants infected with HIV via blood transfusion, blood products or tissue/organ transplant, sexual abuse or persons whose mode of HIV infection was unknown were excluded from the analyses.

Independent variables of interest were age (less than 18 years, 18 – 20 years and 21 – 24 years); race (white, black, other, and unknown); ethnicity (Hispanic/non-Hispanic); highest level of education; smoking status (ever, never); lowest CD4 count in 2006; last CD4 count within 6 months of cervical Pap testing; history of STI (gonorrhea, chlamydia, trichomonas, genital herpes & syphilis), pregnancy (ever, never) and type of clinic where care was received (pediatric only vs. adolescent medicine ± pediatric). HPV infection was not included as an independent variable because it is related to both cervical Pap testing and abnormal cervical Pap results. Racial/ethnic classifications were self-reported by participants.

Statistical Analyses

First, we determined the proportion of the study participants who had at least one and at least 2 documented cervical Pap tests. Among persons who had at least one cervical Pap test done, we determined the prevalence of abnormal Pap test results, categorized into four

groups: atypical cells (ASCUS, ASC-H, ASGUS, AGC-H or atypical cells unspecified); low grade lesions (CIN I, CINII or LSILs); high grade lesions (CINIII or HSILs); or cervical dysplasia unspecified. The most severe diagnosis reported for each subject within the study period was used. We also determined the proportion of abnormal cervical Pap results which had reverted to normal by the end of the study period.

Differences in descriptive characteristics (age, race, ethnicity, highest level of education, smoking, history of other sexually transmitted diseases, parity and site of care) among persons with at least one cervical Pap test done compared to persons with no record of Pap testing were analyzed using the chi-square test and *t* test for normally distributed variables, and the Mann-Whitney *U* test for skewed variables. Co-linearity among variables was evaluated using Pearson's correlation coefficients. Tests of significance were two-tailed and significance was set at 5%.

Generalized linear models (Poisson regressions with robust variance estimates) were used in bivariate analyses to determine the prevalence ratios (PR) for CPAP-S in persons with perinatal versus behavioral HIV infection. In multivariable analysis, generalized linear models (Poisson regressions with robust variance estimates) were used to estimate the adjusted prevalence ratio (APR) for CPAP-S in persons with perinatal versus behavioral HIV infection adjusted for additional factors. The final model included variables identified *a priori* as important (site of care, pregnancy and age) as well as those with *p*-value < 0.05. Ninety-five percent confidence intervals (CI) were constructed for PRs and APRs. To explore the hypothesis of an association between abnormal Pap test results and mode of HIV infection, generalized linear models were used in bivariate and multivariable analysis with the binary outcome of abnormal Pap test results (ever/never) among those with at least one Pap test. The final model included variables with *p*-value < 0.05. All analyses were conducted using Stata Version 10.

Results

Of 408 age-eligible female participants in the LEGACY cohort, 259 participants were sexually active. An additional 28 participants who were not classified as either perinatally or behaviorally HIV-infected were excluded, resulting in a final sample of 231 participants from 20 clinical sites. Two clinics did not contribute any cases to our sample. Among the 231 sexually active HIV-infected females, 46.3% (n=107) were infected with HIV perinatally; 69.3% were black and 20.3% white; and 9.5% were of 'other races (mostly self-reported race as "Puerto Rican"). Twenty seven percent of participants identified themselves as Hispanic (Table 1). Participants ranged in age from 13 – 24 years with a median age of 21 years (Inter quartile range (IQR): 19.5 –23 years) for behaviorally HIV-infected participants and 18 years (IQR: 16 –19 years) for perinatally HIV-infected participants. Forty-six percent of the study population were in high school. Thirteen percent (n=29) had a record of HPV infection, 36.4% (n=84) had a previous STI (gonorrhea, chlamydia, trichomonas, genital herpes & syphilis; including 15 persons also co-infected with HPV), while 51.5 % of the study population had record of ever being pregnant between 2001 and 2006.

Factors associated with cervical Pap testing

At least one cervical Pap test (CPAP-S) was performed in 49% (n=113) of the participants; 38.9% of participants (n=90) had had at least two cervical Pap tests between 2001 and 2006. In bivariate analysis (Table 2), perinatal versus behavioral HIV infection and black versus white race were each significantly associated with decreased likelihood of cervical Pap testing (PR = 0.54; 95% CI 0.40, 0.73 and PR = 0.72; 95% CI 0.55, 0.95, respectively). Age 21 years (compared to <18 years), history of any STI and pregnancy were significantly associated with increased likelihood of cervical Pap testing. Participants managed at clinics with an adolescent medicine specialist on site were 1.2 times as likely to have a cervical Pap test as persons managed at solely pediatric clinics (95% CI 1.02, 1.39). Nadir CD4 count in 2006 was not significantly associated with cervical Pap testing. In multivariable analysis, mode of HIV transmission, race and history of STI remained significantly predictive of cervical Pap testing (Table 2). Participants with perinatal HIV infection were significantly less likely to have had a cervical Pap test compared to those with behavioral HIV infection (APR = 0.66; 95% CI 0.45–0.96). Black race was also independently associated with decreased likelihood of cervical Pap testing (PR= 0.74; 95% CI 0.56–0.96). History of STI was independently associated with an increased probability of cervical Pap screening (APR= 1.56; 95% CI 1.21–2.02).

Among 113 youth with at least one cervical Pap test performed, only 42.5% (48/113) had normal cervical test results. Thirty-seven percent (42/113) of cytology results were classified as low-grade lesions (CIN I, CINII or LSILs) or atypical cells. Approximately 2% of youth (2/113) had high-grade lesions (HSIL or CINIII). No cases of invasive cervical cancer were reported. The specific cytologic results in 18.6% (21/113) of youth were not available (these reports were only noted in medical records as cases of cervical dysplasia). Nineteen percent of abnormal Pap cytology results (12/65) were documented to have reverted to normal at the end of the study period.

Factors associated with abnormal cytology

In bivariate analysis among participants with at least one Pap test, participants of other races (mostly described as “Puerto Rican”) were also almost twice as likely to have an abnormal Pap test report (PR= 1.94; 95% CI 1.11–3.41) compared to whites (Table 3). Participants with CD4 counts of <200 cells/mL within six months of cervical Pap testing (PR= 1.75; 95% CI 1.16, 2.63) and those with an STI diagnosis between 2001 and 2006 (PR= 1.64; 95% CI 1.17, 2.28) had a significantly greater probability of having an abnormal cytology report. Participants receiving care at sites with an adolescent health specialist present were 31% less likely than those cared for at pediatric clinics to have an abnormal Pap test report (PR= 0.69; 0.51–0.94). In multivariable analysis, history of STI and CD4 count nadir <200 cells/mL remained significantly associated with an increased probability of abnormal cervical cytology (PR= 1.94, 95% CI 1.29–2.92 and PR= 2.19, 95% CI 1.26–3.78, respectively) and there was a significant association between site of care and abnormal cytology results (PR= 0.65; 0.42–0.99). We did not find a significant association between mode of HIV infection or race and abnormal cytology results in multivariable analysis.

DISCUSSION

In our cohort of sexually active, HIV-infected female adolescents and young adults (13 – 24 years), we found that only approximately half (49%) of the study population had evidence of having at least one documented cervical Pap test between 2001 and 2006. Although this is much lower than the reported prevalence of cervical Pap testing (81%) in adult HIV-infected women¹⁸, it is consistent with previous reports of lower CPAP-S rates among HIV-infected adolescents¹⁹. This study is the first to compare cervical cancer screening rates in youth with perinatally versus behaviorally acquired HIV infection. Adolescents with perinatal HIV infection in our study population were 34% less likely to have a documented cervical Pap test compared to their behaviorally infected counterparts after adjusting for age, race, type of clinic, pregnancy, and previous STIs. Adolescents with perinatal HIV infection are a unique cohort infected as infants early in the HIV epidemic and who now have survived to reproductive age. Most of these patients have been cared for since infancy in pediatric clinics and may not be perceived as a high-risk group for HPV infection. Recent studies have, however, reported that sexual activity, STIs and pregnancy in this population are common¹⁹ and adoption of an adolescent-centered care model that integrates primary, HIV, obstetric & gynecologic care with mental health, social, and case management services may be necessary for meeting the needs of perinatally (and behaviorally) HIV-infected adolescents²¹.

Another factor which may be contributing to low CPAP-S in this population is the lack of clear guidelines on when to initiate CPAP-S in adolescents with perinatal HIV infection. The American cancer society (ACS) recommends Pap screening for HIV- infected persons at initial HIV evaluation but do not address the timing of initial Pap screening for maturing adolescent patients who acquired HIV infection in infancy. In non-HIV infected young adults, current guidelines recommend cervical cancer screening using the Pap test beginning within three years after the onset of sexual activity or at 21 years of age (whichever comes first), and then every 2–3 years for women aged 30 years if three consecutive annual Pap tests are negative²². It is possible that HIV-infected youth, who are at greater risk of cervical dysplasia, and especially long-term surviving perinatally HIV-infected youth, may need to be approached differently than HIV-uninfected adolescents.

Contrary to the findings of Oster et al¹⁴, we did not find a significant association between increasing age and the likelihood of cervical Pap testing in multivariable analysis. This may be explained by the different age range of participants in the study by Oster et al (median age of 39 years), compared to our study population (median age of 21 years). Consistent with previous reports of racial disparities in cervical cancer screening in the US, blacks were 26% less likely to have had a cervical Pap test compared to whites in our study population. This unfortunate situation may be contributing to the reported racial and ethnic disparities in cervical cancer incidence and mortality rates^{10,23–25} despite an overall decline in cervical cancer incidence and related mortality in the United States. Other studies have found an association between socioeconomic status and cervical cancer screening²⁴ and it is possible this accounts for some of the observed racial disparity in Pap screening in our population.

The high prevalence (57.5%) of cervical dysplasia we found in our population is similar to the 56.4% prevalence reported among 133 females infected with HIV in adolescence in the Reaching for Excellence in Adolescent Care and Health (REACH) cohort²⁶. Others have reported lower rates (20.7%) of cervical Pap smear abnormalities in HIV-infected adolescents²⁷. Although the association between HIV infection and increased risk of HPV-associated cervical malignancy has been well established in previous studies¹⁻⁴, the mechanism through which HIV-related immunodeficiency affects the risk of abnormal cervical cytology is not clear. Some researchers have suggested that the higher rates of HPV and SILs in HIV-infected women are due to HIV-associated CD4 depletion and dysfunction leading to worse outcomes of HPV infection in this population^{28,29}. It has also been suggested that the risk of SIL is directly correlated to the amount of HPV DNA in the cervical tract of women and HIV-related immunosuppression increases the risk of SIL by enhancing HPV replication³⁰. The natural history of HPV infection and the impact of HAART on HPV infection, clearance, and persistence among HIV-infected adolescents is even more complex. Prolonged persistence of HPV has previously been reported among HIV-infected adolescents³¹. Recent studies also show that although HAART increases the life expectancy of HIV patients, it does not appear to have any significant immediate effect on the incidence, clearance, and persistence of high-risk and vaccine-type HPV in HIV-infected adolescents³². Regardless of the mechanism, it is important to recognize the increased risk of cervical dysplasia associated with HIV infection and ensure optimal screening in this population.

Consistent with reported rates among young women in the United States^{5,33}, most cytological abnormalities identified in our study were low-grade lesions. Only two percent of those tested in our study population had high-grade lesions. Some research has suggested that young women with cytologic findings of low-grade squamous lesions can be followed without colposcopy because most of these lesions will resolve without treatment³⁴. However this may not be the case in HIV-infected persons. Moscicki et al in 2004 found a higher incidence of persistent LSIL leading to high-grade squamous intraepithelial lesions in HIV-infected girls compared to HIV-uninfected girls (21.5% vs. 4.8%, respectively) and stressed the need to closely monitor HIV-infected adolescents with LSIL³⁵. In our study population, only 19% of low grade lesions reverted to normal; however, this may be an underestimate of the true rate of reversion of abnormal Paps because our data are based on medical records and not all persons with abnormal Pap results had follow up Pap tests conducted. Both participants with high grade lesions in our population had documentation of reversion to low grade lesions (LDIL & ASCUS) after colposcopy within 6 months – 1 year of diagnosis.

Persons with CD4 count < 200 cells/mL within six months of cervical Pap testing in our population were twice as likely to have had a documented abnormal Pap test result compared with persons with CD4 counts of above 500 cells/mL within the same time frame. This is consistent with the findings of several studies among HIV-infected women that have reported an association between low CD4 counts and an increased risk of developing cervical neoplasia, particularly, high grade lesions³⁶⁻⁴¹. We also found that persons with previous STIs had an increased likelihood of having had a cervical Pap test and were significantly more likely to have an abnormal Pap report. Women with STIs are probably viewed as a high-risk group by clinicians, resulting in a greater likelihood of recommending

cervical cancer screening in this population, in contrast to adolescents with perinatal HIV infection, who may be viewed as a low risk group.

We did not find a significant association between abnormal cervical cytology and mode of HIV infection among persons who had had at least one cervical Pap test. We were, however, considerably under-powered for this sub-group analysis. Since HPV persistence leading to cervical dysplasia has been linked to disordered cell-mediated immune responses and adolescents with perinatal HIV are at a later stage of their HIV continuum (compared to adolescents who acquire HIV during adolescence) when they acquire HPV infection, it is possible that these individuals have a greater risk of developing cervical dysplasia following HPV infection. Further studies are needed to explore this hypothesis and it would be interesting to see if this association is accounted for or remains after adjusting for CD4 counts in other studies.

The strengths of our study include the use of a large multi-site cohort of both perinatally and behaviorally HIV-infected persons representative of sexually active HIV-infected youth receiving care in intermediate and large-sized facilities in the United States. We were also able to use verified medical records of Pap testing instead of relying on self-reported data which is often misleading. The limitations of our study are also recognized. First, as in most studies using abstracted medical records, there was some missing information. In particular, we may not have captured information on Pap tests done on LEGACY participants by providers at non-LEGACY clinic sites. This may have led to some misclassification and underestimation of the prevalence of Pap testing in this population. However, we believe this missing information is minimal because results from tests done elsewhere in HIV-infected persons are usually forwarded to the primary care site. Second, due to the multi-site nature of this study, cytological examination of Pap test samples were conducted by different pathologists in different institutions and some inter-rater variability is possible. To account for this limitation, we classified Pap test results as normal or abnormal and adjusted for site of care in all multivariable analyses. Third, the estimated rates of cervical cytological abnormalities could be misleading if persons who had Pap tests had different sexual risk profiles than those who did not. It would also have been useful to have data on some important potential confounders such as number of lifetime sexual partners, consistent condom use, duration of contraceptive use and socioeconomic status. Finally, our cross-sectional study approach limits our ability to infer a causal relationship between any of our predictor and outcome variables.

The prevalence of cervical Pap screening in our study population of HIV-infected adolescents and young adults was low and it is troubling that cytological abnormalities were detected in more than half who had a cervical Pap test. Our findings do not support the hypothesis that perinatal HIV infection increases the risk of cervical cytological abnormalities; however, there was a strong independent association between perinatal route of HIV infection and decreased likelihood of cervical Pap testing. Interventions targeted at HIV-infected adolescents and their care providers are needed to improve cervical Pap screening in this population. Having survived HIV this far, it would be unfortunate if women perinatally infected with HIV suffer morbidity or death from preventable diseases like cervical cancer. Every effort should be made to prevent this through routine screening.

Prevention of HPV acquisition through HPV vaccination may be even more beneficial among adolescents perinatally infected with HIV. Our findings underscore the importance of regular cervical cancer screening in HIV-infected young female adults. Clearer guidelines on initiation and frequency of cervical Pap screening in adolescents with perinatal HIV infection may be needed.

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Contributed patient data to:

*2006 cohort only

**All LEGACY cohorts

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Table 1

Socio-demographic and Clinical Characteristics of HIV-infected Adolescent Females, LEGACY Study, United States, 2006 (n=231)

Characteristic	N	%
Mode of HIV infection		
Behavioral [*]	124	53.7
Perinatal ^a	107	46.3
Race		
White	47	20.3
Black	160	69.3
Other	22	9.5
Unknown/missing	2	0.9
Ethnicity		
Non-Hispanic	167	72.3
Hispanic	64	27.7
Age, years		
<18	54	23.4
18 – 20	92	39.8
≥ 21 years	85	36.8
Educational level		
Up to Jr. High/ Middle school	41	17.8
High school	106	45.9
Graduated high school or GED	30	13.0
College or vocational school	28	12.1
Unknown/missing	26	11.2
STIs^β		
No STI	147	63.6
Any STI	84	36.4
Pregnancy[‡]		
Never Pregnant	112	48.5
Ever pregnant	119	51.5
CD4 nadir		
≥ 200 cells/μl	186	80.5
<200 cells/μl	45	19.5
Type of clinic		
Pediatric	51	22.1
Adolescent medicine specialist on site	180	77.9
At least 1 Pap test done[‡]	113	48.9

GED = General Educational Development

* Behavioral = IV drug use + Consensual sexual activity

α Perinatal = Perinatal transmission + transmission from breastfeeding

β Syphilis, gonorrhea, herpes, trichomonas or Chlamydia diagnosis between 2001 and 2006

\dagger Between 2001 and 2006

Table 2

Bivariate & Multivariable analyses (generalized linear models) - Pap testing among HIV-infected Adolescent Females, LEGACY Study, United States, 2006. (n=231)

Characteristic	N	Pap tests Done, n (%)	Bivariate		Multivariable	
			PR α	95% CI	APR β	95% CI
Mode of HIV infection						
Behavioral	124	77 (62.1)	ref		ref	
Perinatal	107	36 (33.6)	0.54*	0.40 – 0.73	0.66*	0.45–0.96
Race						
White	47	30 (63.8)	ref		ref	
Black	160	74 (46.3)	0.72*	0.55–0.95	0.74*	0.56–0.96
Other	22	9 (40.9)	0.64	0.37–1.11	0.76	0.44–1.33
Unknown/missing	2	0 (0.0)	-		-	
Ethnicity						
Non-Hispanic	167	80 (47.9)	ref			
Hispanic	64	33 (51.6)	1.07	0.80–1.43		
Age, years						
<18	54	19 (35.2)	ref			
18 – 20	92	45 (48.9)	1.39	0.91–2.11	1.09	0.71–1.69
21 years	85	49 (57.7)	1.64*	1.09–2.46	1.10	0.96–1.74
Educational level						
Up to Jr. High/ Middle school	41	19 (46.3)	ref			
High school	106	55 (51.9)	1.11	0.76–1.61		
Graduated high school or GED	30	14 (46.7)	0.94	0.55–1.59		
College or vocational school	28	13 (46.4)	0.98	0.58–1.64		
STI^{†,***}						
No previous STI	147	59 (40.1)	ref		ref	
Any STI	84	54 (64.3)	1.60*	1.24 – 2.06	1.56*	1.21–2.02

Characteristic	N	Pap tests Done, n (%)	Bivariate		Multivariable	
			PR ^a	95% CI	APR ^b	95% CI
Pregnancy**						
Never Pregnant	112	45 (40.2)	ref			
Ever Pregnant	119	68 (57.1)	1.42*	1.08–1.87	1.04	0.76 – 1.41
CD4 Nadir						
200 cells/ μ l	186	93 (50.0)	ref			
<200 cells/ μ l	45	20 (44.4)	0.89	0.62–1.27		
Type of clinic						
Pediatric	51	18 (35.3)	ref			
Adolescent. medicine specialist on site	180	95 (52.8)	1.19*	1.02 – 1.39	1.13	0.73 – 1.74

GED = General Educational Development CI = Confidence Interval

* Prevalence Ratio

^a Adjusted Prevalence Ratio

^b P value < 0.05

[†] Syphilis, gonorrhea, herpes, trichomonas or Chlamydia diagnosis

*** Between 2001 and 2006

Table 3

Bivariate & Multivariable analyses (generalized linear models) - Abnormal Pap Tests among HIV - infected Adolescent Females with a Cervical Pap Test, LEGACY Study, United States, 2006 (n=1113).

Characteristic	N	Abnormal Paps, n (%)	Bivariate		Multivariable	
			PR α	95% CI	APR β	95% CI
Mode of HIV transmission						
Behavioral	77	42 (54.6)	ref		ref	-
Perinatal	36	23 (63.9)	1.17	0.85–1.61	0.93	0.61–1.41
Race						
Whites	30	12 (40.0)	ref			
Blacks	74	46 (62.2)	1.55	0.97–2.49	1.05	0.65–1.70
Other race	9	7 (77.8)	1.94*	1.11–3.41	1.42	0.61–2.87
Ethnicity						
Hispanic	33	17 (51.5)	0.85	0.58–1.25		
Age (years)						
<18 years	19	10 (52.6)	ref			
18 – 20 years	45	28 (62.2)	1.18	0.73–1.92		
21 years	49	27 (55.1)	1.05	0.63–1.72		
STI[†]						
No STI	59	26 (44.1)	ref		ref	
Any STI	54	39 (72.2)	1.64*	1.17–2.28	1.94*	1.29–2.92
Pregnancy^{**}						
Never Pregnant	45	29 (64.4)	ref			
Ever Pregnant	68	36 (52.9)	0.82	0.60–1.12		
CD4 count^{ca}						
>=500 cells/ μ l	40	20 (50.0)	ref		ref	
200–499 cells/ μ l	54	28 (51.9)	1.04	0.69–1.55	1.21	0.82–1.78
<200 cells/ μ l	8	7 (87.5)	1.75*	1.16–2.63	2.19*	1.26–3.78

Characteristic	N	Abnormal Paps, n (%)	Bivariate		Multivariable	
			PR ^a	95% CI	APR ^b	95% CI
Type of clinic						
Pediatric	18	14 (77.8)	ref		ref	
Adolescent med. specialist on site	95	51 (53.7)	0.69*	0.51–0.94	0.65*	0.42–0.99
Smoking						
Never	51	30 (58.8)	ref			
Ever	32	18 (56.3)	0.96	0.65–1.40		
missing	30	17(56.7)	-			

CI = Confidence Interval

* Prevalence Ratio

^a Adjusted Prevalence Ratio

^b P value < 0.05

[†] Syphilis, gonorrhea, herpes, trichomonas or Chlamydia diagnosis

** Between 2001 and 2006

^{αα} Last CD4 count within 6 months of cervical Pap testing