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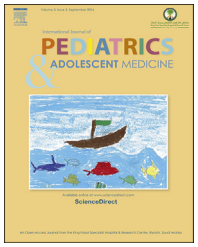

Original Research Article

Adolescent HIV viral load in an urban hospital in Newark, New Jersey

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Abstract *Background and objectives:* Human immunodeficiency virus (HIV) in adolescents is a growing concern. Amid psychosocial challenges, adolescents must successfully transition into adult-centered care; however, little is known about outcome measurements within this period. We assessed the trend in adolescent HIV viral loads (VLs) in a community with a high HIV prevalence, allowing physicians to better recognize the challenges of transitioning adolescents with HIV to adult care.
Patients and methods: All HIV RNA VLs from the Molecular Virology Lab at University Hospital in Newark, New Jersey, from 2007 to 2010 were obtained. Patients were divided into pediatric (<13 years of age), adolescent (13–25 years of age), and adult (>25 years of age) age groups. Univariate and multivariate analyses assessed characteristics of patients by age and gender.
Results: A minimum of 40 pediatric, 178 adolescent, and 1335 adult patients were identified per year. There was a statistically significant increase in VLs of adolescents when compared

Abbreviations: HIV, human immunodeficiency virus; STIs, sexually transmitted infections; AIDS, acquired immune deficiency syndrome; CDC, centers for disease control and prevention; WHO, World Health Organization; VL, viral load; HAART, highly active antiretroviral therapy; ART, antiretroviral therapy; NIH, National Institutes of Health; NCI, National Cancer Institute.

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to pediatric patients ($P < .02$). In 3 of the 4 years, there was a statistically significant increase in the rate of male adolescents reaching undetectable VLs compared to female adolescents. The average VL by age demonstrated increasing VLs from age 12 through age 24, while the percentage of patients reaching undetectable VLs peaked at 80% at age 8 and declined through age 24.

Conclusion: Successful transitional care programs should focus on pediatric needs to address the noticeable decrease in virologic control beginning at 8 years of age and the decreased rate of virologic suppression in females, creating concern for potential gender inequalities and increased risk of vertical transmission.

1. Introduction

Human immunodeficiency virus (HIV) in the adolescent community is an increasing concern. Globally, there are more than 2 million adolescents living with HIV [1]. Adolescents often engage in high-risk sexual behavior, and individuals aged 15—19 have the highest reported rates of sexually transmitted infections (STIs). Among high school students in 2013, 46.8% have had sexual intercourse, 34% were currently sexually active, and 48.9% of the currently sexually active students did not use a condom the last time they had sexual intercourse. Nationwide, while 85.3% of students had been taught about acquired immune deficiency syndrome (AIDS) or HIV infection in school, only 12.9% of students had ever been tested for HIV [2]. Centers for Disease Control and Prevention (CDC) estimates the 9961 youth aged 13—24 years who were diagnosed with HIV infections in 2013 represents 21% of the total diagnoses that year. Around the same time, there were an estimated 62,400 youth living with HIV infection, with over half undiagnosed [3]. In sub-Saharan Africa, only 10% of young men and 15% of young women aged 15—24 were aware of their HIV status. The World Health Organization (WHO) estimates that adolescent deaths from HIV are rising, which is assumed to be from the lack of support and care that they receive after childhood [1].

During this time, adolescents are facing challenges with their own physical changes, brain development, and social milestones. This period of transition significantly impacts an adolescent's ability to take ownership of their health and successfully enter adult-centered care. In the 2013 CDC HIV Surveillance Report, the lowest percentage of HIV patients to establish linkage of care by age group was persons aged 13—24 years (73.4%) and the lowest percentage to be retained in HIV medical care was persons aged 25—34 years (46.7%) [4]. While many papers and medical organizations recognize the importance of capturing this patient population and preparing them for adulthood, very little has been published regarding outcome measurements of chronic diseases within this phase of adolescent transition. Several programs are being developed to address this very fragile period for young adult health, but understanding the current outcomes in chronic disease during adolescence is necessary for understanding the effectiveness of any transitional care program.

By reviewing the HIV Viral Load (VL) data from University Hospital in Newark, New Jersey, we assessed the trends in adolescent HIV VLs and virologic control in an urban community with a high HIV prevalence. Knowledge of these trends will allow physicians around the world to better recognize the challenges of transitioning young adults with HIV to adult-centered care and identify areas to target in the development of appropriate transitional care programs.

2. Patients and methods

All HIV RNA VLs from the Molecular Virology Laboratory at the University Hospital in Newark, New Jersey, from 2007 to 2010 were obtained. The study received expedited review and approval by the Rutgers New Jersey Medical School Institutional Review Board. Patients were divided into pediatric (age <13 years), adolescent (age 13—25 years), and adult (age >25 years) groups, all of whom were receiving treatment at University Hospital's HIV clinic. The clinic is located in the Francois-Xavier Bagnoud Center and is funded in part by the Ryan White Grant Program. Through social services, the clinic provides access to medication assistance programs, housing programs, and mental healthcare to all patients at point-of-care. Clinic staff consists of two board-certified pediatric infectious diseases physicians, two nurses, one advanced practice nurse, one psychologist, and two social workers. Patients are typically scheduled for 3-month follow-up visits; however, those patients requiring more intense therapy are given more frequent appointments. Most patients were retained in the clinic and were not transitioned out. Over 95% of pediatric patients were infected prenatally and many have grown up attending the clinic. During the time period of the study, all were offered highly active antiretroviral therapy (HAART) with the majority receiving protease inhibitors. Some patients were receiving complex multi-tablet regimes due to multiple past virologic failures with 3-class resistance.

The mean viral load was calculated as the average of each individual's viral load tests over a calendar year. Undetectable viral loads were assigned a value of half the lower limit of detection, and high viral loads were assigned the maximum limit of detection. Undetectable viral loads were defined as <400 copies/mL, which was the most frequent lower limit of detection used in 2001—2008. Patients were considered undetectable if they averaged an

undetectable viral load over the calendar year. Univariate and multivariate analyses were performed to assess characteristics of patients by age and gender.

3. Results

A minimum of 40 pediatric, 178 adolescent, and 1335 adult patients were identified per year. There were no statistically significant differences in the mean ages of the three groups over the four-year time period.

Males comprised 37–47% of the pediatric patients, 48–57% of the adolescent patients, and 54–57% of the adults. Over 95% of the clinic's HIV patients were prenatally infected, and over 90% were actively accepting HAART.

Based on October 2010 performance measures, 75% of patients had two clinic appointments at least 3 months apart, 66% of patients had no less than two CD4 count measurements, 95% of patients with CD4 counts <200 received PCP prophylaxis, 91% of patients with AIDS received HAART, 67% received syphilis screening, and 81% received tuberculosis screening. Lower performance rates were recorded for cervical cancer screening in only 23% of eligible patients. Performance data did not include age and therefore could not be categorized into age cohorts.

The average viral loads from 2007 to 2010 were lowest for pediatric patients, next lowest for adolescents, and highest for adults (Table 1). This demonstrated a statistically significant increase in the mean viral load in adolescents when compared to pediatric patients (42% increase, $P < .02$) and in adults when compared to adolescents (195% increase, $P < .0002$). The pediatric population had the highest percentage of patients reaching undetectable VLs (58–72.6%). The adolescent group (34.9–54.5%) and the adult group (42.5–52.7%) were not significantly different over the four years (Fig. 1).

In 3 of the 4 years, there was a statistically significant increase in the percentage of male adolescents reaching undetectable VL compared with female adolescents (Fig. 2). Of note, 2009 was the only year in which the mean viral load in females was lower than that of the males.

Reviewing average VL by age demonstrates an increasing VL from age 12 through age 24, while the percentage of patients reaching undetectable VL peaks at 80% at age 8 and begins trending down through age 24 (Fig. 3).

4. Discussion

Data from University Hospital showed evidence of worsening virologic control by age group. Over the four years analyzed, the average viral load of pediatric patients was lower than that of the adolescent population, which in turn was lower than that of the adult population. Within the declining trend, the pediatric population had a significantly higher rate of patients averaging undetectable VLs compared with the adolescent and adult populations. The latter populations were not significantly different with regards to percentage of patients with undetectable VLs in comparison to each other. In a study by Ellen et al, almost 30% of youth with HIV in 14 cities were found to have significantly high VLs, associated with high rates of transmission [5]. This troubling trend highlights the potential challenges during adolescence that make treating and preventing disease more difficult. Agwu et al found a similar trend in patients with perinatally acquired HIV in clinics across the United States – older age, black race, and Hispanic ethnicity were associated with increased risk of advanced immunosuppression and detectable viremia [6]. During adolescence, patients are undergoing puberty, learning how to be autonomous young adults, and feeling challenged by increasing responsibilities with more complex external pressures [7]. While easily influenced by their environment, peers, and mentors, these young adults are developing behavioral foundations that will last their life time. These foundations subsequently impact their ability to independently manage their own health, including safer-sex practices, disease recognition, medication compliance, and prioritizing care.

When breaking this down further and examining mean VL by age from birth to 25 years of age, there is notable evidence of worsening virologic control and decreasing percentage of patients averaging undetectable VLs. The decrease in adolescent patients reaching undetectable viral load levels coincides with the average age of first sexual activity and could be related to the high rates of new HIV infections in this age group. Without proper counseling and care, these young adults are at significant risk of acquiring and perpetuating the spread of HIV. Additionally, given the challenges of an inner city environment, these patients must tackle their health concerns with limited resources and assistance. Yet another barrier to adolescents with HIV is its unique burden of stigma, relationship to poverty, infection rates within families, and its prevalence within ethnic minorities [8]. As Andiman states, "Stigma intersects with nearly every other factor and, as experienced in social networks, leads many youth to mistrust individuals outside of their closest social circles, sometimes including their [healthcare providers]." Especially in the adolescent period when self-perception and development of self-confidence is of high priority, having to confront and carry a stigma during this period can lead to self-doubt and conflict: "when adolescents fail to know or share their HIV status, they cannot become autonomous." [7].

Given these concerns, many programs and associations urge the creation of multifaceted transitional care initiatives and specifically target the transition of an adolescent in their early 20s. However, based on the virologic results in this urban population, declining virologic control was noted as young as 8 years of age. This would suggest that transitional care programs should be initiated at a much younger age and not necessarily focus on just the transfer of clinical care, but it should focus more on the psychosocial challenges of adolescence and young adulthood. Within the clinic studied, all patients are assessed annually for social work and mental health needs, have access to psychosocial

Table 1 Average viral load by year and age group.

	2007	2008	2009	2010
Pediatric	5357	7532	1885	12,248
Adolescent	37,683	27,117	10,836	17,404
Adult	57,120	53,252	36,580	51,344

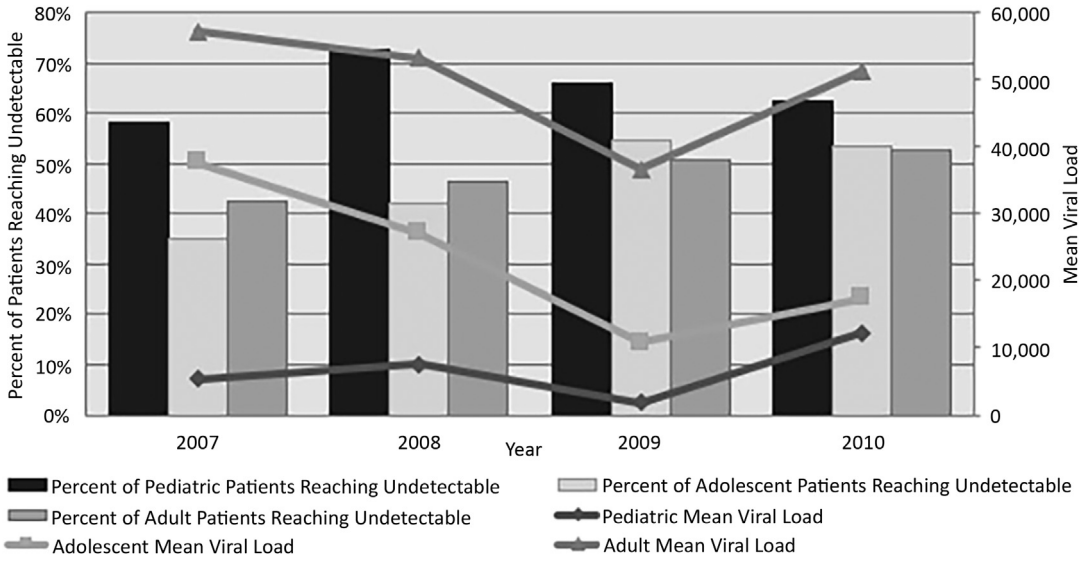

Figure 1 Percent of patients reaching undetectable and average viral load by age grouping.

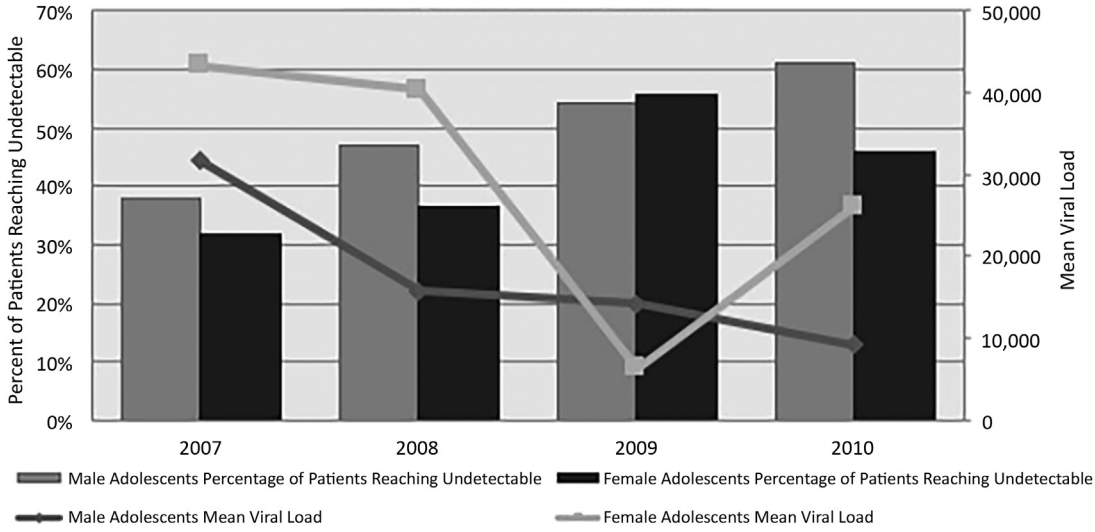

Figure 2 Percent of adolescent patients reaching undetectable and average viral load by gender.

assistance, and no services provided are restricted by age. Despite extensive social and mental health services, the decline in undetectable VLs in the adolescent population suggests identifying more specific adolescent needs. In a review of the Adolescent Trials Network for HIV/AIDS Interventions, researchers were surveyed on various aspects of their transitional care programs. Several clinics stated that transitions to adult care should occur between 22 and 24 years of age; however, discussions about when transitioning should begin was variable from as early as age 16 to as late as age 24. There were also discrepancies between how a "successful transition" was measured — "informants … were unable to accurately report an outcome" [9]. Some barriers to monitoring outcome included the lack of tracking mechanisms, while more anecdotal measures of success included emotional maturity, functional independence, available support systems, and stable health, and housing benefits [9]. Given the young age at which declines in virologic control was noted, these data would suggest a transitional care program starting at the age of 8 years and likely aimed at barriers seen in young adolescence and not just late adolescence.

The significant decline in virologic control by age observed in this study would also suggest that further investigations are needed to correlate adolescent perceptions of healthcare independence and virologic control. While virologic control over time has largely been affected by new advancements in antiretroviral therapy (ART), medication adherence, and understanding barriers to this remains tantamount to the success of any program. In a study looking at self-reported HIV-medication adherence of 12—19-year olds, only 28.3% of patients had taken all of their medications in the previous month, citing changes in one's day-to-day routine and forgetting to take medications as the most common barriers [10]. Another study performed at the National Institutes of Health (NIH) and National

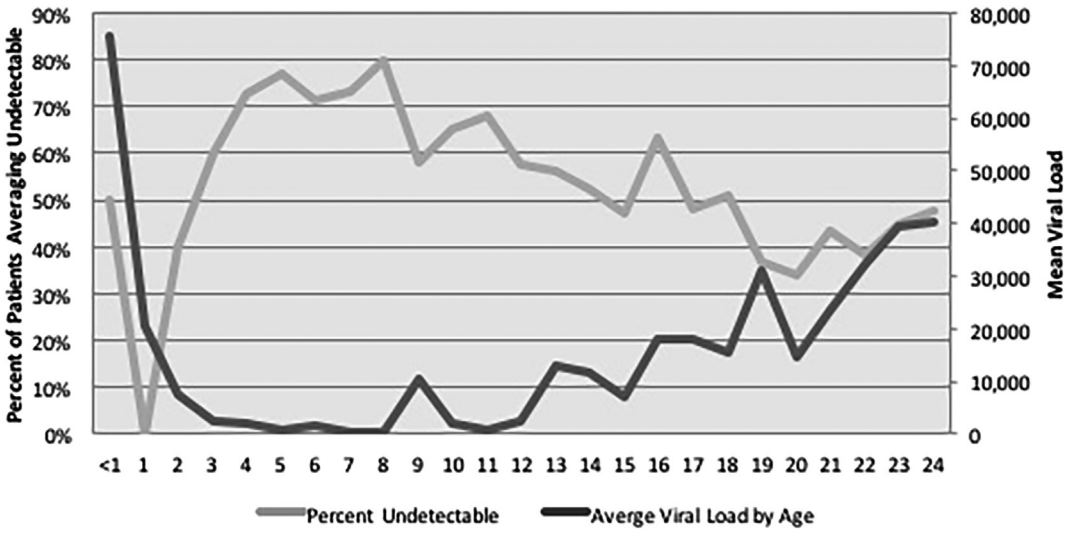

Figure 3 Percent of pediatric and adolescent patients reaching undetectable viral load and mean viral load by age.

Cancer Institute (NCI), looked at changes in adolescent readiness over a 6-month period within a closing clinical research program. Demographics as well as CD4 cell count and HIV-1 RNA levels were measured 6 months apart in addition to completion of an anxiety scale and readiness questionnaire. After barriers to transition were addressed by the medical provider and social worker, the results showed no significant difference in CD4 cell counts and HIV-1 RNA levels, but there was a significant reduction in anxiety and increased confidence in their home community physician, social worker, and knowledge of disease and medications [11]. These studies suggest that adolescent education regarding their medications, side effects, and general care is key in developing a successful program in medication adherence and understanding, however, it may not result in better HIV outcomes. An early review of the Transition Readiness Assessment created by the national "Got Transition" program and given to adolescents in the pediatric subspecialty clinics at University Hospital showed good adolescent understanding of disease, emergencies, and medications, but it showed poor understanding of general healthcare navigation. Even in early adolescence, however, virologic data from University Hospital indicates that more longitudinal studies are needed to objectively measure these transitional outcomes and correlate successful education with virologic control.

Also concerning is that in 3 of the 4 years examined, the viral load in adolescent females and the number of female patients averaging undetectable VLs demonstrated worsening virologic control than that of their male counterparts. Additionally, based on the 2010 performance rates in the clinic, only 23% of adolescent females received a cervical cancer screening. In the 2009—2013 CDC data, rates of infection for female adults and adolescents actually decreased [12]; however, based on the above findings, one can question if the healthcare system within this area is able to deliver optimal care to females versus males. The Enhancing Communication to Improve HIV Outcomes (ECHO) study revealed that HIV providers had more negative perceptions of female personality characteristics than male and felt more frustrated with female patients than male. Women were also shown to be less educated or unemployed and more likely to report medication nonadherence and depressive symptoms [13]. In New Jersey, women had an HIV infection rate of 14.2 per 100,000 persons, compared with 9.3 in New York and 5.6 in Connecticut [14]. Adolescent girls and young women (15—24 years) are twice as likely to be at risk of HIV infection compared to boys and young men in the same age group worldwide [15]. Given this observed inequality, it is possible that transitional care programs aimed at treating this population may need to factor in gender inequalities psychologically, socially, or otherwise.

It is also important for women to recognize that heterosexual contact accounted for 25% of all diagnosed HIV infections in the United States and 86% of those infections in adolescent and young adult women with HIV, and perinatally acquired infections accounted for an estimated 107 new infections in 2013 [14,15]. Globally, HIV/AIDS is the leading cause of death among women aged 15—44 years [15]. While maternally acquired HIV has been dramatically reduced through the use of aggressive screening and treatment, scattered cases remain. University Hospital had at least one maternally acquired case of HIV in each year of this data set. Subsequently, with poor virologic control, females of child-bearing age in this study could represent a future increase in maternally acquired HIV cases in Newark.

These data looked at viral load analysis performed in one lab at one urban university hospital during a four-year span and, consequently, is confounded by small sample sizes, particularly in the first few years of life. The population is also heterogeneous in terms of treatment, mode of acquisition, and stage of disease. While the majority of pediatric and adolescent patients in our study have prenatally acquired HIV, we were unable to separate out the small number of behaviorally acquired patients who may have different risk factors and behavioral patterns. Thus, a more in-depth study looking at the means of transmission should follow. Other demographic information would also be helpful in obtaining a closer look at the gender differences, as well as rates of medication compliance, clinic follow-up patterns, psychosocial barriers to care, and adolescent-perceived attitudes

and knowledge of HIV and disease management. The recent addition of the Transition Readiness Assessment to adolescent care will reveal self-perceived adolescent understanding of disease and healthcare management. Extensive review of these assessments and other programs in adolescent care is required to further isolate barriers to optimal treatment. Additionally, we do not account for the increase in efficacious HIV medications and treatment strategies during the time period of this study.

5. Conclusion

Pediatric patients develop a noticeable decrease in virologic control as they enter their adolescent years, which coincides with the onset of high-risk sexual activity. This increased viral load in infected patients puts others at higher risk and may contribute to adolescents having the fastest growing rate of new HIV infections. The decreased rate of virologic suppression in females of child-bearing age is also concerning as it presents an increased risk of vertical transmission. The development of adolescent HIV clinics, with dedicated services and transitional care programs focused on the unique needs of this population early in their adolescence, is one potential method of improving virologic control in this high-risk group.

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