Abstract # 534
Poster Session: P-05
21st Conference on Retroviruses and Opportunistic Infections
March 3-6, 2014
Boston, MA

Dynamics of HPV in Romanian Women Infected with HIV During Early Childhood

Luminita Ene[1], Cristina Voinea[1], Claudia Stefanescu[1], Diana Sima[1], Dan Duiculescu [1,2], Sanjay R. Mehta[3,4]

"Dr.Victor Babes" Hospital for Infectious and Tropical Diseases, Bucharest, Romania; Titu Maiorescu" University Bucharest, Romania; University of California San Diego, La Jolla, CA, USA

Sanjay Mehta, MD
University of California, San Diego
9500 Gilman Drive MC 8208
San Diego, CA 92093, USA
E-mail: srmehta@ucsd.edu

Background

•Screening for cervical cancer is not standard of care in Romania, and 90% of Romanian women aged 15-44 have never been screened for CC [(1)]
•HPV is more commonly detected and more aggressive in HIV infected individuals [(2,3)], possibly due to a combination of increased susceptibility, increased viral persistence, and reactivation of infection.[(4)]
•Since most HIV infected women acquire HPV infection prior to HIV, some HPV specific immune responses may have already developed prior to infection with HIV.
•The dynamics of HPV infection may be potentially much worse in women who acquire HIV before HPV

Objective

To examine the prevalence and dynamics of HPV infection in a cohort of young Romanian women (22-25 years in age) infected with HIV during early childhood

Methods

Study Design

•A case-control study to evaluate the differences in HPV detection, cervical pathology and viral dynamics between young women infected with HIV during early childhood and HIV un-infected women

Study Populations

•65 Romanian women (22-25 years in age) parenterally infected with HIV during early childhood followed at Victor Babes Hospital in Bucharest, Romania with no previous history of cervical cancer
• 25 age-matched control subjects from a gynecology clinic at the Victor Babes Center for Diagnosis

Baseline Assessment

•All participants had a history and physical including a pelvic exam with samples taken for Papanicolau cytology and cervical cell sampling for HPV (Roche® Linear Array HPV Genotyping Test)
•High Risk HPV subtypes were defined using the WHO/IARC guidelines
• All participants underwent STI screening (syphilis, chlamydia, gonorrhea, candida, bacterial vaginosis, and trichomonas) and pregnancy testing
• All subjects were given a questionnaire eliciting demographic data, information about illicit drug use, alcohol use, smoking, and detailed sexual behavior (i.e. timing of sexual debut, number and sex of all partners, type and timing of sexual acts, and use of protection/contraception

Follow up Assessment

•HIV infected participants returned for f/u STI screening, cytology and HPV screening between 6 months and 1 year after the initial visit

References

1. Romanian Family Health Initiative cervical cancer component 2003-2006
2. Akarolo-Anthony SN, et al. *BMC Infect Dis* 2013; 13(1): 521.
3. Zhang YX, et. Al. *Zhonghua Fu Chan Ke Za Zhi* 2012; 47(3): 185-90
4. Strickler HD, et al. J Natl Cancer Inst 2005; 97(8): 577-86

Results

Table 1. Baseline Characteristics of the Study Population

		HIV Infected (n=65)	HIV Uninfected (n=25)	p value
Demographics				
Mean Age (years)		23.1 +/- 1.1	22.5 +/- 1.1	**0.01**
Education	<= 12 years	70.8% (46)	8% (2)	**<0.001**
	>12 years	29.2% (19)	88% (22)	
Sexual Orientation	Heterosexual	100% (65)	100% (25)	ns
Married		20% (13)	4% (1)	ns
Work Status	Student	18.5% (12)	72% (18)	**<0.001**
	Employed	18.5% (12)	24% (6)	
	Unemployed/Social Support	63% (41)	0	
Residence	Urban	64.6% (42)	96% (24)	0.06
	Rural	35.4% (23)	4% (1)	
Social Behaviors				
Alcohol Use		38.5% (25)	64% (16)	ns
Tobacco Use		64.6% (42)	52% (13)	ns
Illicit Drug Use		0	12% (3)	ns
Sexual History				
Mean Age at Sexual Debut (years)		18.1	17.8	ns
Median # of partners		2	2.5	ns
Median # of Episodes of Sexual Intercourse in last month		1	6	**0.001**
Condom Use		81.5% (53)	100% (25)	0.056
Depression episodes		20% (13)	0	**0.007**
HIV History				
Risk Factor for Acquisition	Parenteral (non-IDU)	87.7% (57)		
	Transfusion	7.7% (5)		
	Unknown	4.6% (3)		
On cART		100% (65)		
Mean CD4 Nadir (T-cell count)		188		
Mean CD4 at Baseline Visit (T-cell count)		610		

•HIV infected subjects were slightly younger, less educated, and more likely to be on social support.
•HIV infected subjects were less sexually active, but also less likely to use condoms.

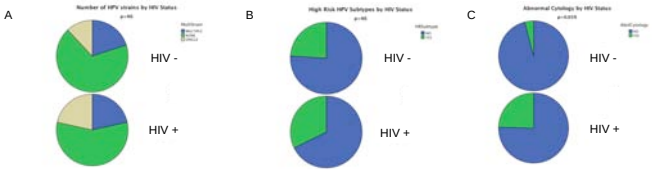

Figure 1. A. Proportion of HIV infected and uninfected individuals with single vs. multiple subtype HPV infection. **B.** Proportion of individuals with high risk subtypes. **C.** Proportion of individuals with abnormal cervical cytology at baseline visit.

•HIV infected and uninfected subjects had similar rates of HPV infection, high risk HPV subtypes, and multiple subtype infection.
•However, HIV infected subjects had significantly higher rates of abnormal cervical cytology (25.3% vs. 4.6%).

Table 2. Characteristics of Co-Infected Subjects

		HIV/HPV Co-infection (28)	HIV infection alone (37)	P value
Demographics				
Mean Age (y)		23.3 +/- 1.6	23 +/- 0.8	ns
Education	<=12y	19	27	ns
	>12y	9	10	
Sexual History				
Mean Age at Sexual Debut (y)		17.8	18.4	ns
Median # of Partners (IQR)		2 (1.75-3.25)	2 (1-2.25)	0.05
Mean # of Episodes of Sexual Intercourse in last month		1.0	1.7	0.06
Condom Use		89.3%(25)	75.7%(28)	ns

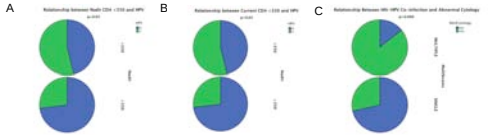

Figure 2. A. Proportion of HIV infected w/ and w/o HPV infection with CD4 nadir <200 **B.** Proportion of HIV infected w/ and w/o HPV infection with current CD4 <200. **C.** Proportions of co-infected individuals with and without multiple HPV subtypes with abnormal cytology.

•Nadir and current CD4 counts <350 are associated with more HPV infection (p=0.05 and p=0.02 respectively).
• Co-infection with multiple strains of HPV is associated with more abnormal cytology (p=0.006).

• An annual incidence of 0.69 HPV strains per year in HIV infections was observed.
• Acquisition of new strains was associated with lower nadir and current CD4 counts.
• **30% of newly acquired strains were preventable with a quadrivalent HPV Vaccine**

Conclusions

•HPV infection occurred in women with controlled HIV infection at similar rates as in controls but was associated with higher rates of cervical pathology
•The presence and acquisition of HPV infection is associated with lower nadir and current CD4 counts in HIV infected individuals.
• Given the availability of safe, immunogenic and effective vaccines, even resource-limited countries should consider providing HPV vaccination for all young women infected with HIV.

Acknowledgments

This study was funded by the University of California, San Diego Center for AIDS Research (P30 AI036214).