Antibody Response to HPV Vaccination in Pediatric and Adolescent People Living with HIV (PLWH)

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Introduction

•Immune dysfunction related to HIV infection is associated with inability to clear HPV infection and increased risk of HPV-related malignancies. The HPV vaccine is recommended for PLWH, but its efficacy and long-term immunogenicity in perinatal HIV patients need further investigation as the HIV- associated immune dysfunction may blunt the vaccine response. We assessed the antibody (Ab) response to quadrivalent HPV vaccine Gardasil® (4vHPV) in a cohort of young PLWH, most having perinatally acquired.

Methods

•PLWH on combined antiretroviral therapy (cART), between 7.8 and 20.6 years old, males and females were offered the 3-dose 4v HPV series between 2007 and 2017. All consented patients attending this clinic had blood samples collected for a research archive when this can be accomplished from the same venipuncture used for a clinical indication.

•Plasma IgG titers to HPV 6 (H6), 11 (H11), 16 (H16) and 18 (H18) were measured using multiplex VLP-based ELISA with parallel line analysis and reported as International Units (IU)/ml (for H16 and H18) or arbitrary units (AU)/ml (for H6 and H11). The median + 2 standard deviations of the Ab titer in negative children's sera used as cut-off for seropositivity. Other epidemiologic and clinical data was obtained from medical records. Cut off values were as following: 0.5 AU/ml (H6), 0.3 AU/ml (H11), 1.4 IU/ml (H16) and 2.4 IU/ml (H18).

•This analysis was restricted to the 36 participants with archived plasma prior to vaccination (baseline – sample 0) and samples post dose 1. All participants had 3 post-vaccine samples (samples 1, 2 & 3). All participants received 3 doses of 4vHPV. Median interval from 1st dose to 2nd and 3rd doses of 4vHPV were 73 and 216 days. Sample 1 was collected at median of 91 days after dose 1, sample 2, 169 after dose 2 and sample 3, 740 after dose 3. Sample 4 was available for 26 patients, median 2327 days after dose 1. Rank-sum test, X^2 or Fisher's Exact Test were employed.

• We requested and received Committee for the Protection of Human Subjects (CPHS) permission to apply 4v HPV from 7 years old to both males and females at the time the vaccine was first available to the clinic. Blood samples for this study were obtained under the CPHS archive review.

Results

Table 1: Demographic Characteristics, Baseline HPV status (prior to vaccine) and overall response to different serotypes

	Baseline* seropositive to any serotype	Baseline* seronegative to all serotypes	p-value
Subjects (n)	10 (28%)	26 (72%)	
Age in years, median (min – max)	16 (8.8-20.7)	12 (7.9-18.9)	0.007
Gender, female	5 (50%)	18 (66%)	0.454
Ethnicity, Black	9 (90%)	15 (58%)	0.217
	Baseline* seropositive to specific serotypes	**Baseline* seronegative to specific serotypes**	**Seroconversion post-vaccination****
At least 1 serotype			100%
H6	7 (19%)	29(81%)	97%
H11	7 (19%)	29 (81%)	100%
H16	6 (17%)	30 (83%)	97%
H18	5 (14%)	31 (86%)	87%
H6,11,16 &18	3 (9%)	33 (91%)	85%

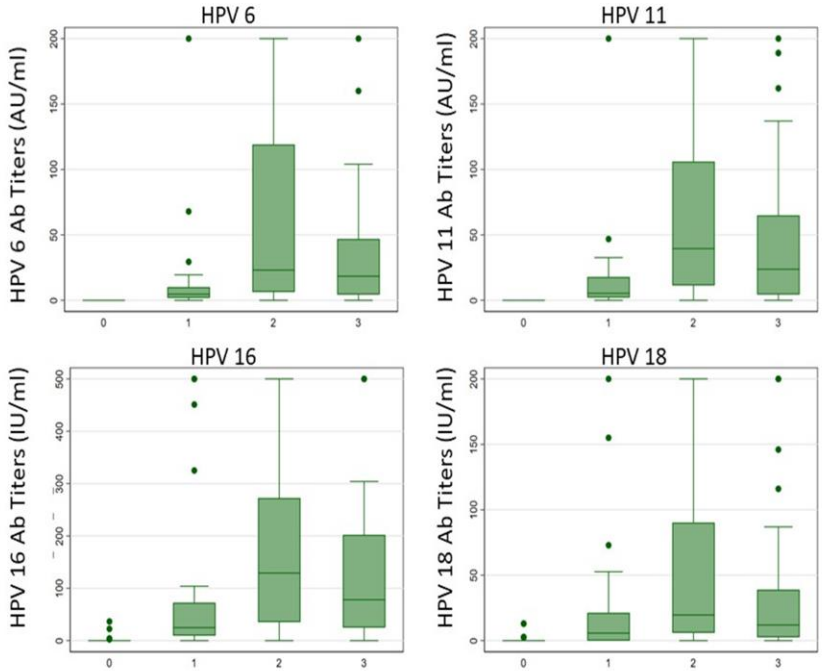
*Baseline represents before first dose of 4vHPV
**in those with negative baseline antibody to the corresponding serotype(s), seroconversion that happened at any post-vaccine sample.

Table 2: HIV markers in responders and non-responders to HPV vaccination (to all 4 serotypes)

	Responders to all serotypes	Non-responder to all serotypes	p-value
Subjects (n)	22	4	
Viral load, copies/ml, median	101	12 920	0.05
CD4%, median	29	36	0.8

• Older patients and Black patients were more likely to be seropositive prior to immunization. (Table 1) Most patients mounted Ab to all 4 serotypes with least response to H18. Viral load was higher in those who did not seroconvert to all 4 serotypes. CD4% (Table 2), age, gender and ethnicity were not significantly different compared to those who had Ab response. Peak response for all 4 serotypes occurred after dose 2.

Figure 1: Box and Whiskers Plots Graphs representing Ab response to the 4 HPV types



• 26 patients had a 4th sample post-immunization (2.3 to 9 years from dose 3, median 5.7). Of these 26, 19 patients who were seronegative to all serotypes at baseline seroconverted post-immunization to at least 1 serotype, 6 of which lost their Ab to some serotypes (see Figure 2). These 6 patients had higher VL (median 9100, IQR 2180-131360) compared to the ones who remained seropositive over time (median 48, IQR 48-760). Gender, ethnicity, CD4 count and duration between sample 4 and vaccine dose 3 were similar in both groups.

Conclusions

• In the complex environment of a pediatric HIV specialty clinic, most PLWH mounted Ab responses to 4v HPV that were durable. H18 was least immunogenic. Patients with higher HIV VL were less likely to seroconvert for all types and were more likely to serorevert.

Figure 2: Hierachy Diagram Representing Patients with ADistant Plasma Sample (Sample 4)

26 patients had additional sample 4

7 were seropositive to at least 1 serotype at baseline

All 19 who were seronegative at baseline seroconverted post-immunization to at least 1 serotype and remained seropositive at sample 4

6/19 lost Ab to some serotypes

Patterns of anti HPV Ab in Participants Seroreverting at Median 5.7 years

	HPV Type			
Pt	H6	H11	H16	H18
1	+	+	+	-
2	-	-	-	-
3	-	-	-	-
4	-	+	-	-
5	+	+	+	-
6	-	-	+	-

Symbols: + antibodies present; - antibodies not detected (black never seroconverted, red seroreverted