Determining the Efficacy of the Gardasil-9 Vaccine in HIV-Positive Individuals

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Objectives

- Conduct the study on a diverse population of non-vaccinated, partially vaccinated, and fully vaccinated against HPV
- Determine specific HPV genotypes found in anogenital tract of HIV infected people positive with HPV

Background/Intro

High-risk oncogenic Human papillomaviruses (HPV) cause the majority of anal and cervical cancer [3]. Most often, persistent HPV infections can lead to pre-cancerous lesions, such as low or high-grade dysplasia that can morph into cancer over time (Figure 1) [2,4]. Gardasil 9 is an effective vaccine in preventing HPV-related diseases [1] Most studies regarding vaccine efficacy of Gardasil 9 have centered around immunocompetent individuals. Some studies have been done to determine the effectiveness of the HPV vaccine in HIV-positive individuals, most often showing an antibody response for previously vaccinated individuals [5,6] but there are few studies done that observe this response in a diverse background of individuals before and after receiving the Gardasil-9 vaccine.

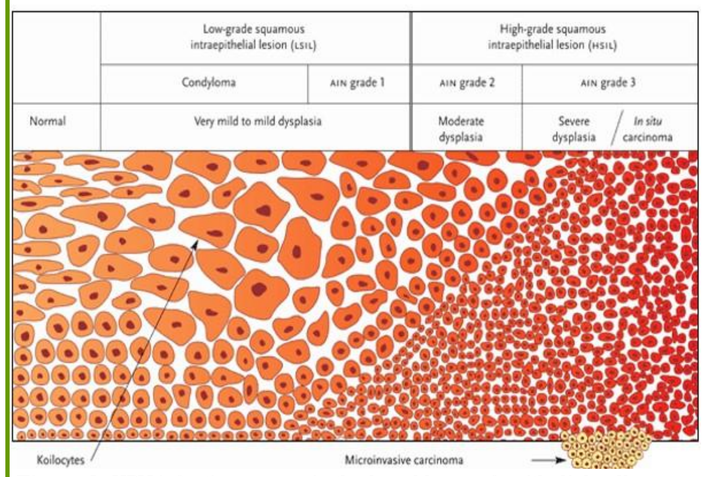

Figure 1. HPV infection occurs in the basal layer of epithelial cells - oftentimes dysregulating epithelial differentiation for viral replication. This leads to low-grade dysplasia in HPV-infected regions, which could advance to high-grade dysplasia and become cancer cells if not treated early.

Enrollment Criteria

- **Approximately 150 HIV-positive adults, under informed consent, were enrolled in the study at the University Medical Center (UMC) with the following:**

Inclusion Criteria

- A blood CD4+ T cell count of **≥ 200 cells/mL**
- HIV viral load <1000 genome copies/mL
- If taking antiretroviral medicine then stable on it for **≥ 3 months**

1st Cohort

- Not previously and/or partially vaccinated with Gardasil before enrollment

Anogenital swab on vaccine Naive → **Receive Vaccine series** → **Anogenital Swab post vaccination**

2nd Cohort

- **Previously received all 3 doses of the Gardasil vaccine**

Low recruitment of HPV vaccine naive individuals led to another sector of enrolled individuals. People with all three doses of the HPV vaccine get swabs of DNA taken from the anogenital region for HPV genotyping and testing of their antibodies. Follow-ups occur every 6 months for more swab extracts.

We hypothesize that the previously vaccinated cohort will have lower rates of HPV positivity than the previously unvaccinated/partially vaccinated cohort.

Results

Characteristics	Vaccinated	Unvaccinated	p-value
Sample Size (n, %)	28(100)	22(100)	
Age (avg, range)			p=0.14
<40	16(57%)	8(36%)	
≥40	12(43%)	14(64%)	
Gender (n, %)			p=0.60
Female	10(36%)	6(27%)	
Male	18(64%)	15(68%)	
Race (n, %)			p=0.44
White/Caucasian	3(11%)	5(23%)	
Black/African American	24(86%)	17(77%)	
Other	1(4%)	0	
HPV Results (n,%)			p=1.11
HPV positive	9(32%)	12(55%)	
Other Factors			
Alcohol Consumers (n,%)	15(54%)	18(82%)	p=0.036
Cigarette Smokers (n,%)	10(36%)	9(41%)	p=0.71
Employed (n,%)	8(29%)	10(46%)	p=0.17
Insured(n,%)	27(96%)	22(100%)	

Population Characteristics

- Sample size is 50
- HPV positivity between unvaccinated and vaccinated prior to enrollment showed no statistical significance
- Alcohol consumption in unvaccinated and vaccinated cohorts showed statistical significance
- The majority of the sample population was:
  - Black/African American
  - Men
  - Insured

Table 1. Listed Demographics of the total individuals that have been tested for HPV, broken down by age, race, gender, HPV positivity/negativity, and outside factors. A chi-squared test was used to test statistical significance between HPV-positive and HPV-negative tested individuals - the p-values from the test are listed. The only statistical significance found was from alcohol consumption between the two prospective cohorts.

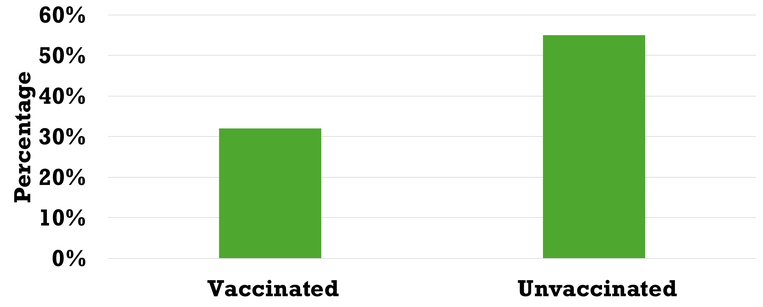

Figure 2. A bar chart of the percentage of previously vaccinated and unvaccinated people before enrollment that expressed HPV-positivity. While no significance was observed, there is a difference within the cohorts, as more than half of the unvaccinated showed positivity compared to the vaccinated.

Methods

PCR

Primer Sets	Size Fragment	
HPV L1 gene	448bp	MY11→ 5' – GCM CAG GGW CAT AAY AAT GG – 3'
		MY09→5' – CGT CCM ARR GGA WAC TGA TC – 3'
β-globin	268bp	PCO4→5'– GAA GAG CCA AGG ACA GGT AC – 3'
		GH20→5'– CAA CTT CAT CCA CGT TCA CC – 3'

Table 2. A dual primer PCR was completed on the extracted swab DNA from the anal and vaginal region. MY09/MY11, a degenerate primer set, was utilized to detect various HPV genotypes from the sampled Genomic DNA. A β-globin primer set, PC04/GH20, was used to make sure human DNA was present.

Gel Electrophoresis

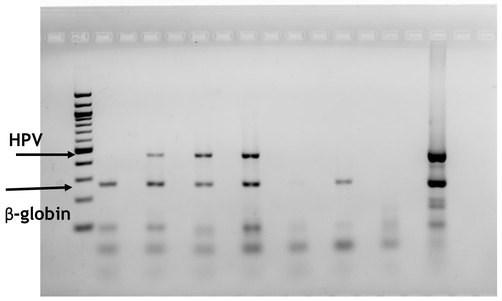

Figure 3. Gel Electrophoresis was utilized to separate the DNA fragments from the dual primer PCR. Negative and positive controls were also ran under the same analysis with the cohort samples to ensure quality of the results.

Discussion

- A trend of higher rates of HIV-positivity seen in the cohort that was unvaccinated against Gardasil-9 prior to enrollment
  - Maybe due to a discrepancy in which HPV- genotypes Gardasil-9 targets
  - Gardasil-9 targets, types 6, 11,16, 18, 31, 33, 45, 52, and 58 [3]
- People living with HIV have a higher chance of developing and being diagnosed with different forms of cancer, including HPV [4]
- People infected with HIV are 19x more likely to develop anal cancer and HIV-positive women are 3x more likely to develop cervical cancer [4]
- HIV-positive individuals are more likely to die from cancer compared to the general public[4]
- There are known outside factors such as smoking and alcohol use that greatly increases the chances of HIV infected people develop cancer [4]

Future Directions

- This study will continue to progress with the extraction and testing of the rest of the swab samples
- HPV positive samples will be sent for genotyping through My-Seq Platform
- A comparison will likely be done with non-immune deficient population data to note any discrepancies

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