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HPV Vaccination Status and COVID-19 Symptomatology

B. A. Bedard, MPH[1,3,4], E. Penrose, MS[2], P. A. Pettit, MSL[2,3], K.N. Voos, BS[2], K.Ohlson, RN, BSN[2], C. Wahls, RN, BSN[2], K. Shuknecht, RN, BSN[2]

[1]Genesee and Orleans County Health Departments
[2]Genesee County Health Department
[3]The College at Brockport Department of Public Health, Adjunct Faculty
[4]Nazareth College Department of Public Health, Adjunct Faculty

***Corresponding author:** Brenden A. Bedard, MPH, Genesee and Orleans County Health Department, 3837 W. Main St. Rd., Batavia, NY 14020, USA, Tel: +1-585-589-2873
Email: Brenden.Bedard@co.genesee.ny.us

Abstract

From March 17to 20 October20, 2020, the Genesee County Health Department (GCHD) investigated 295 COVID-19 cases in residents located outside of federal facilities. Through medical records and patient interviews, GCHD collected the patients' symptoms, both those at onset and those experienced prior to and on the day of interview/hospital presentation. Of the patients investigated during this time frame, 81 were born during or after 1990; of this age cohort, GCHD determined each case's HPV vaccination status. The symptoms self-reported by patients during the course of their COVID-19 illness were used to compare the severity of illness and types of symptoms experienced by both the vaccinated and the non-vaccinated group. We found that the HPV-vaccinated group was statistically significantly less likely to experience cough, muscle aches and fatigue. Having received the HPV vaccine seemed to significantly increase the likelihood that the infected case would experience no symptoms at all P (.019).

Keyword: *COVID-19, Vaccinated, HPV, HPV vaccine, medical records, patients*

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Introduction

In December 2019, cases of pneumonia of unknown etiology began to appear in Wuhan, Hubei, China.[1] By January 24, 2020, cases had been discovered in other Chinese provinces as well as Thailand, Japan, South Korea, and the United States.[1] The first known COVID-19 case in New York State, which was travel-related, was reported on March1, 2020 in New York City.[2] From that point on, the disease began an apparent northward and westward spread throughout the state of New York, with the first cases north of the Hudson Valley reported on March 7th in Saratoga County.[3] The largest urban areas in Upstate New York, Monroe County (Rochester) and Erie County (Buffalo), reported their first COVID-19 cases on March 12th and March 15th respectively.[4-5]

Description of the Situation in Genesee County, New York

Genesee County is located in rural Western New York, roughly halfway in between the cities of Buffalo and Rochester, and has a population of 57,280.[6] Shortly after those two urban areas detected their first COVID-19 cases, Genesee County received its first positive test result in a resident on March 17th. The resident had extensive travel history to neighboring Monroe County, and is believed to have likely contracted the disease there.

From March17 through October 20, 2020, Genesee County received 347 positive COVID-19 test results of individuals living within the county. Of those patients, 49 were detainees at the Buffalo Federal Detention Facility, and three were residents at Batavia Veterans Affairs Medical Center. The Genesee County Health Department interviewed and monitored the remaining 295cases.

Reported COVID-19 cases in Genesee County among non-Federal residents peaked on April 7, with a one-day high of 12 new positive community cases. Two cases reported onset dates of 7 March representing the earliest known cases in Genesee County, and self-reported dates of onset among cases peaked from March 19 through 23, having slowly decreased and then leveled off during the summer months, followed by an increase in September and October 2020.

Human Papillomavirus (HPV) and Cross-reactivity with coronaviruses

HPV has been shown to be cross-reactive to the NS2 protein from the coronavirus which has produced an antiviral immune response indicated by cytokine production.[7]Cross- reactivity and cross-protection for the HPV prophylactic vaccine and an HPV therapeutic vaccine has been shown to produce T cell responses.[7,8]Immunizations have shown cross-reactivity and cross-protection to antigens other than those contained in the vaccine.[9]The authors looked at this literature and wanted to see if there was a potential for a protective immune response from the HPV vaccine towards SARS-CoV-2.

Method

The first HPV vaccine, Gardasil-4, was licensed in the United State in 2006.[10] This vaccine protected against four strains of HPV- 6, 11, 16 and 18.[10]In 2009, the FDA approved a two strain vaccine, Cervarix, that protects against types 16 and 18.[11]In 2014, the FDA approved the nine strain vaccine, Gardasil-9, which included protection against the original four strains of HPV from Gardasil-4 and added strains 31, 33, 45, 52 and 58.[12]

In August 2006, Article 21, Title 6, of Public Health Law 2168 was signed into law.[12]This law mandates the creation of a statewide immunization registry where New York State providers collect and store vaccination records on all persons less than 19 years of age.[12]The immunization registry in New York State is called the New York State Immunization Information System (NYSIIS). The public health law mandated that as of 1 January 2008 all current immunizations administered on all persons less than 19 years of age, along with their past immunization histories must be entered into NYSIIS within 14 days of administration.[13]

Of the 347 patients investigated by the Genesee County Health Department during the seven-month period, 81 cases were born during or after 1990. Based on this 30-year review we hoped to capture everyone who was vaccinated with the HPV vaccine that would be mandated to be reported into NYSIIS.

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Using NYSIIS we were able to determine that, of these81 cases, 45were vaccinated for HPV and 36had no record of having been vaccinated for HPV. All vaccinated individuals received at least one dose of Gardasil-4, Gardasil-9, or Cervarix. The demographics of the vaccinated and unvaccinated groups were similar in age, varied in some respects by racial breakdown, and varied markedly by sex. The vaccinated group individuals were born between 1990 and 2008 (median 1999) and the unvaccinated group individuals were born between 1990 and 2019 (mean 1996).

In the vaccinated group, 68.89% of individuals self-identified as white, 15.56% as Latino, 6.67% as Black, 4.44% Native American, and 4.44% as more than one race, whereas in the unvaccinated group, 63.89% self-identified as white, 25.00% as Latino, and 11.11% as Native American. (See Table 1.) The vaccinated group was more predominantly female (68.89%) than the unvaccinated group (52.78%), likely reflecting the fact that anHPV vaccine was not approved for men until 2009, and at that point only in men for the prevention of genital warts.[14]

Table 1: Demographics of Genesee County COVID-19 cases born in 1990 or later by HPV vaccination status

	Age		Race					Sex	
	Age Range	Median Age	White	Latino	Black	Native American	More than One Race	Male	Female
Vaccinated Group (45)	1990-2008	1999	68.89% (31)	15.56% (7)	6.67% (3)	4.44% (2)	4.44% (2)	31.11% (14)	68.89% (31)
Unvaccinated Group (36)	1990-2019	1996	63.89% (23)	25.00% (9)	0	11.11% (4)	0	47.22% (17)	52.78% (19)

An analysis was performed using Epi Info Version 7.2. The two tailed Fisher's exact tests and two-by-two tables were developed to determine a significance P-values at<0.05. This statistical analysis categorized the group into non-HPV vaccinated COVID-19 cases compared with HPV vaccinated COVID-19 cases associated with COVID-19 symptoms. Table 2 describes the COVID-19 cases based on symptoms and vaccination status with the HPV vaccine. Our results indicate that there were three significant symptoms that the vaccine seemed to protect against.

These symptoms are cough P (.0127), muscle aches P (.0234) and fatigue P (.0445). Because cough, and fatigue in particular are some of the most common symptoms of COVID-19 that our cases have reported, a significant reduction in those symptoms due to HPV vaccination would be more impactful for patients than a significant reduction in an uncommon symptom. Additionally, having received the HPV vaccine seemed to significantly increase the likelihood that the infected case would experience no symptoms at all P (.0019).

Table 2: COVID-19 Symptoms and HPV Vaccination Status

Not Vaccinated with HPV				Vaccinated HPV				Fisher Exact
Symptoms	Yes	No	Total	Symptoms	Yes	No	Total	p < .05
Fever	14	22	36	Fever	9	36	45	0.0833
Cough	27	9	36	Cough	21	24	45	0.0127
Productive Cough	4	32	36	Productive Cough	8	37	45	0.5338
Shortness of Breath	12	24	36	Shortness of Breath	9	36	45	0.2075
Chills	17	19	36	Chills	15	30	45	0.255

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Headache	23	13	36	Headache	27	18	45	0.8193
Muscle Aches	21	15	36	Muscle Aches	14	31	45	0.0234
Back Pain	11	25	36	Back Pain	7	38	45	0.1175
Vomiting	4	32	36	Vomiting	2	43	45	0.3986
Abdominal Pain	6	30	36	Abdominal Pain	6	39	45	0.7108
Diarrhea	16	20	36	Diarrhea	11	34	45	0.096
Nausea	8	28	36	Nausea	11	34	45	1
Loss of Taste	16	20	36	Loss of Taste	16	29	45	0.495
Loss of Smell	17	19	36	Loss of Smell	15	30	45	0.255
Sore Throat	17	19	36	Sore Throat	18	27	45	0.6521
Dehydration	12	24	36	Dehydration	6	39	45	0.0578
Fatigue	23	13	36	Fatigue	18	27	45	0.0445
Chest Pain	5	31	36	Chest Pain	10	35	45	0.3985
Wheezing	4	32	36	Wheezing	3	42	45	0.6941
Runny Nose	19	17	36	Runny Nose	16	29	45	0.1754
Congestion	16	20	36	Congestion	18	27	45	0.8212
Altered Mental Status	3	33	36	Altered Mental Status	1	44	45	0.3181
Symptomatic	35	1	36	Symptomatic	35	10	45	0.019

Conclusion

Our findings indicate that these results should be looked at from a larger population perspective to see if the HPV vaccine can produce some cross-reactivity and protect against some COVID-19 symptoms, possibly lessening the severity of this illness for those vaccinated. This could be important with new variants of SARS-CoV-2 and low COVID vaccination rates. Additional laboratory studies should be conducted to see if there is cross-reactivity of the HPV virus where T-cells recognized naturally processed and presented epitopes from SARS-CoV-2 infected cells. The authors are not advocating to not get the COVID vaccine but to also get the HPV vaccine for the potential of cross-reactivity with SARS-CoV-2.Limitations to this study include a small sample of data, and the potential that providers did not input historical vaccines into NYSIIS when the New York State mandate came out in 2008.

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