

EFFECT OF COVID-19 PANDEMIC RESPONSE MEASURES ON ACUTE RESPIRATORY PATHOGEN INCIDENCE AT A NEW YORK CITY CANCER CENTER

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Introduction

The SARS-CoV2 pandemic has resulted in a unique scenario with respect to the transmission of upper respiratory tract pathogens. In the beginning of March 2020, emergency measures were implemented in New York City to curb the spread of the SARS-CoV2 virus, including closure of schools and non-essential businesses, adherence to social distancing guidelines, and the recommendation that individuals wear face coverings. The mode of transmission of SARS-CoV2 is similar to the mode of transmission of other acute upper respiratory pathogens. Therefore, it is hypothesized by this study that there would be a decrease in acute respiratory pathogen detection in the Memorial Sloan Kettering Cancer Center patient population after the onset of the Covid-19 pandemic in comparison to previous years. This retrospective cohort study consists of MSKCC patients receiving a multiplex respiratory pathogen PCR test from August 1, 2014 until July 31, 2020. Data was cleaned so that each unique patient was counted once per year per, counting a positive result for a respiratory pathogen if they tested positive. This study investigates the effect the COVID-19 pandemic had on other respiratory viruses; therefore COVID-19 test results are omitted from the study. Using March 22, 2020 as the time of exposure the 2019-2020 viral year is compared to the previous 5 years for both a pre-exposure group and a post-exposure group using multivariable logistic regression. A large reduction in the odds of testing positive for a respiratory virus were observed for most pathogen categories.

Methods

Data was extracted from the MSKCC laboratory informatic system (LIS) databases, deidentified, and compiled into a database for statistical analysis. Test results were treated as belonging to a particular viral year in order to capture each viral season. The seasonality of respiratory pathogens has been well established with influenza, coronavirus, and RSV prevailing in winter and early spring months, rhinovirus and para influenza viruses peaking in spring and fall, and adenovirus prevailing year-round. In order to account for the natural seasonal variability in respiratory pathogen prevalence, the 2019-2020 viral season will be compared to the same time period in previous seasons.^{9, 10} Each viral year was defined as August 1 to July 31 of the following year. To better estimate disease incidence and to remove duplicate testing, the data was cleaned so that each unique patient's test result for each pathogen was only counted once per viral year, counting the positive result if they tested positive that year. This study investigates the effect the COVID-19 pandemic had on other respiratory viruses; therefore COVID-19 test results are omitted from the study. The testing methodology of all test results in the data set were the film array respiratory pathogen multiplex PCR panel produced by bioMerieux as well as an influenza and RSV multiplex PCR test produced by Cepheid.

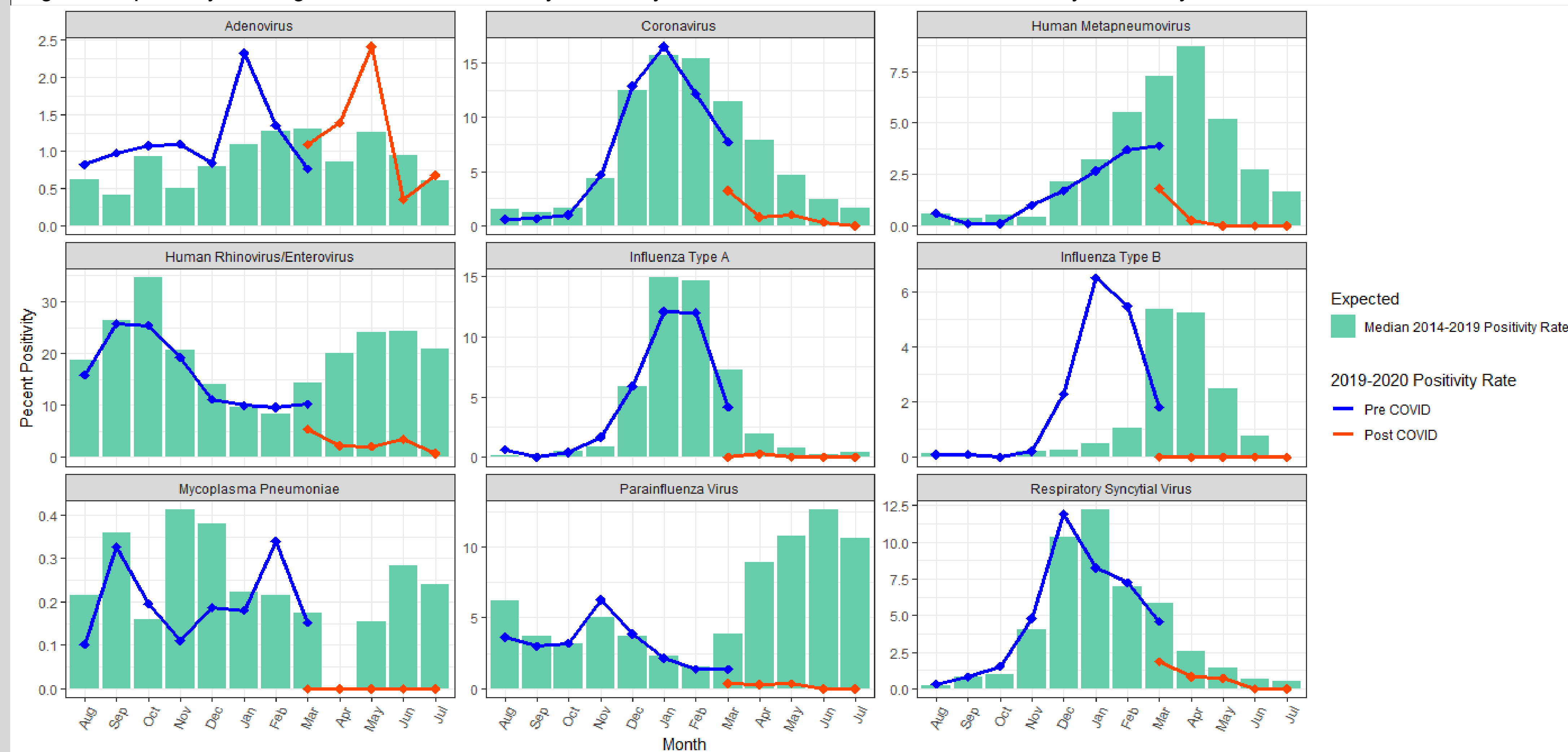
To determine if there was a decrease in the rate of respiratory pathogens after COVID-19 pandemic mitigation interventions were put in place on March 22, 2020, the data were divided into three exposure groups. The first group, the reference group, included all test results from August 1, 2014 until July 31, 2019, encompassing 5 viral seasons. The second group, the pre-exposure group, includes all test results from August 1, 2019, the beginning of viral year 2019-2020, until March 22, when the implementation of COVID-19 mitigation strategies occurred. The third group is the post-exposure group consisting of all test results from March 23 2020 until July 31, 2020. These 3 time periods were coded in the data set as "1" for the reference group, "2" for the pre-exposure group, and "3" for the post-exposure group. Chi square tests for association between the demographic characteristics of sex, age, and race and either a positive or negative result were performed (Table 1).

Methods (Cont.)

Multiple binary logistic regressions using test result (positive or negative) as the response variable and "time period" as the explanatory variable while controlling for sex, age, and race, were then independently performed between the pre-exposure group (period 2) and the reference group (period 1) as well as the post-exposure (period 3) group and the reference group (period 1) for the corresponding time periods for each pathogen. This means that the pre-exposure group, results from August 1, 2019 – March 22, 2020, is being compared to results from August 1 – March 22 for each previous year going back to 2014. Similarly, the post-exposure group, results from March 23, 2020- July 31, 2020, is being compared to results from March 23- July 31 for each previous year going back to 2015. For the post-exposure regression models for Influenza B and Mycoplasma pneumoniae, Firth's Bias-Reduced Logistic Regression was performed to correct for the complete separation introduced into the model due to zero cases of positive results for these pathogens during the post-exposure time period. All data analysis was performed using R Studio statistical software.

Results

Fig. 1 Respiratory Pathogen 2019-2020 Monthly Positivity Rates vs Median 2014-2019 Monthly Positivity Rates



Results

Table 1. Population Characteristics and Respiratory Pathogen Test Positivity by Period

	2014-2019			Aug 1 - March 22 2019-2020			March 22-July 31 2019-2020							
	Positive (%)	Total	P	Positive (%)	Total	P	Positive (%)	Total	P					
Sex														
F	5849	4.9	119586	1515	4.2	35960	<0.001	7115	4.9	145989	53	0.7	7067	<0.001
M	6074	5.5	110491	1636	5.1	31933		7468	5.5	136996	42	0.7	6406	
Age														
<18	1804	14.0	12919	430	13.5	3179	<0.001	2084	13.9	14956	20	5.1	394	<0.001
18-65	5667	5.3	107869	1599	4.6	34771		6809	5.2	131669	38	0.5	6926	
>65	4452	4.1	109289	1122	3.7	29943		5690	4.2	136360	37	0.6	6173	
Race														
White	8681	5.1	171221	2275	4.6	49863	<0.001	10647	5.0	211018	69	0.7	10101	<0.001
Black Or African American	1117	5.2	21587	320	4.8	6603		1373	5.2	26362	14	1.1	1310	
Asian-Far East/Indian Subcont	1012	5.7	17620	252	4.3	5838		1206	5.5	21753	7	0.6	1119	
Unknown	652	5.3	12204	124	5.1	2439		799	5.5	14516	4	0.9	450	
Other	461	6.2	7445	180	5.7	3150		558	6.0	9334	1	0.2	513	
Total														
Total			230077			67893				282985			13493	

Note: Counts of positives and totals are counts of tests not of individual patients. P-Values correspond to chi square tests. * 7 inconclusive and 68 equivocal test results deleted from dataset.

Table 2. Table 2. Respiratory Pathogen Positivity Rates and Odds Ratios Pre and Post COVID-19

Pathogen	Aug 1 - March 22			March 22-July 31		
	Positive (%)	Total	OR (95% CI)	Positive (%)	Total	P
Adenovirus						
2014-2019	227	0.9	25709	1.40	(1.09, 1.79)	0.006
2019-2020	90	1.2	7540			
Coronavirus						
2014-2019	2084	8.1	25588	0.92	(0.84, 1.01)	0.072
2019-2020	562	7.5	7539			
Human Metapneumovirus						
2014-2019	688	2.7	25562	0.62	(0.51, 0.74)	<0.001
2019-2020	124	1.6	7543			
Human Rhinovirus/Enterovirus						
2014-2019	4626	18.4	25088	0.87	(0.82, 0.93)	<0.001
2019-2020	1203	16.0	7542			
Influenza Type A						
2014-2019	1529	5.9	25707	0.81	(0.72, 0.90)	<0.001
2019-2020	365	4.8	7543			
Influenza Type B						
2014-2019	334	1.3	25688	1.64	(1.36, 1.98)	<0.001
2019-2020	163	2.2	7548			
Mycoplasma Pneumoniae						
2014-2019	70	0.3	26758	0.75	(0.42, 1.28)	0.322
2019-2020	15	0.2	7547			
Parainfluenza Virus						
2014-2019	929	3.7	25281	0.87	(0.76, 1.01)	0.061
2019-2020	239	3.2	7545			
Respiratory Syncytial Virus						
2014-2019	1436	5.6	25696	0.93	(0.83, 1.04)	0.238
2019-2020	390	5.2	7546			
Total						
2014-2019	11923	5.2	230077	0.90	(0.87, 0.94)	<0.001
2019-2020	3151	4.6	67893			

Note: Totals are total number of tests not total number of individual patients. In each pathogen category the 2014-2019 time period is the referent group. * 7 inconclusive and 68 equivocal test results deleted from dataset.

Results

Population characteristics appear in Table 1. Chi square tests showed significant association for sex, race, and gender with respiratory virus positivity. Males appear to have higher positivity for respiratory virus than females. Pediatric patients had significantly higher percent positivity rate for respiratory viruses than patients older than 18. White and black/ African American patients did not have significantly different proportions of infections but the proportion of infections of these groups was significantly lower than the other racial groups considered in the model. In order to visualize the seasonality and comparison of positivity rates, monthly positivity rates for each pathogen were calculated. The median positivity rate for the 2014-2019 months were plotted as columns while the pre-exposure and post-exposure groups of 2019-2020 were plotted as lines on top of the 2014-2019 group as seen in Figure 1. Comparing the pre-exposure group of 2019-2020 to the reference group of 2014-2019 using multiple logistic regression showed no statistical difference in odds for coronavirus, Mycoplasma pneumonia, parainfluenza virus, and respiratory syncytial virus. The odds of testing positive for influenza B or adenovirus were higher in the pre-exposure period of 2019 than in the 5 years prior, whereas the odds of testing positive for human metapneumovirus, human rhinovirus/ enterovirus, and influenza A for the same period comparison were reduced. For the post-exposure group comparison, the odds of testing positive for all pathogens was significantly reduced compared to the previous 5 years except for adenovirus which showed no significant difference in the odds of testing positive.

Discussion

This study has several limitations. Firstly, it is an observational study that measures association and therefore cannot establish causation between exposure and outcome. Additionally, this study cannot account for potential changes in testing practices that may have occurred as a result of the Covid-19 pandemic. It is possible that the rate of positive respiratory pathogen tests went down because any individual exhibiting acute upper respiratory disease isolated and ruling out Covid-19 was the priority rather than detecting other respiratory viruses. MSKCC as well as all other institutions made efforts to have patients as well as staff stay at home as much as possible. The volume of testing was significantly reduced in the post-exposure group compared to previous years. This would not be expected to drastically change the positivity rate for respiratory viruses but there is potential for bias as a result. Finally, this study has no way of determining which Covid-19 measure was responsible for the observed decrease in odds of testing positive for a respiratory virus in the post exposure group. This study provides valuable data that can be used to guide infection control practices in a post pandemic cancer center environment. The observed decrease in odds of an individual in the patient population testing positive for almost all of the most common respiratory pathogens provides evidence that could be used to justify retaining some of the infection control practices that were employed during the pandemic in order to curtail all respiratory infections as well as future outbreaks of SARS-CoV2.

Faculty Advisor

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References

1. New York State. (2020, March 22). Governor Cuomo Issues Guidance on Essential Services Under the "New York State on PAUSE" Executive Order. Ny. Gov. <https://www.governor.ny.gov/news/governor-cuomo-issues-guidance-essential-services-under-new-york-state-pause-executive-order>
2. Partridge L, McCreery E, Cheema R, et al. Evaluation of Seasonal Respiratory Virus Activity Before and After the Statewide COVID-19 Shelter-in-Place Order in Northern California. *JAMA Network Open* 2021;4(3):e2030281.
3. Kuitunen L, Antama M, Mäkelä J, et al. Effect of Social Distancing Due to the COVID-19 Pandemic on the Incidence of Viral Respiratory Tract Infections in Children in Finland During Early 2020. *Pediatr Infect Dis J* 2020;39(12):e429-e7.
4. Chu H, Chu H, Tai T, et al. Impact of Wearing Masks, Hand Hygiene, and Social Distancing on Influenza, Enterovirus, and All-Cause Pneumonia During the Coronavirus Pandemic: Retrospective National Epidemiological Surveillance Study. *J Med Internet Res* 2020;22(8):e21257.
5. Pransky S, Reifler K, Rossi M, et al. COVID-19 mitigation strategies were associated with decreases in other respiratory virus infections. *Open Forum Infectious Diseases* 2021.
6. Monto AS. Epidemiology of viral respiratory infections. *Am J Med* 2002;112 Suppl 6A:45-125.
7. Dasaraju PV, Liu C. Infections of the Respiratory System. In: Baron S, editor. *Medical Microbiology*. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 93. Available from: <https://www.ncbi.nlm.nih.gov/books/NB68342/>
8. Thom KA, Kleinberg M, Roghmann MC. Infection prevention in the cancer center. *Clin Infect Dis* 2013;57(4):579-85.
9. Moriyama M, Hugentobler W, Iwasaki A. Seasonality of Respiratory Viral Infections. *Annual Review of Virology*. 2020;7(1):83-101. doi:10.1146/annurev-virology-012420-023405
10. Litwin CM, Bosley JG. Seasonality and prevalence of respiratory pathogens detected by multiplex PCR at a tertiary care medical center. *Arch Virol*. Jan 2014;159(1):65-72. doi:10.1007/s00705-013-1794-4