COVID-19 Serology Analysis Hematology and Oncology Patients

Bureau of Epidemiology

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DEPARTMENT OF HEALTH

Executive Summary

Background

COVID-19 is a respiratory virus more likely to cause severe disease among older adults and people with acute and chronic health conditions. The Centers for Disease Control and Prevention (CDC) has listed cancer, immunocompromised state, and blood disorders as pre-existing health conditions associated with more severe illness requiring hospitalization, intensive care, mechanical ventilation, and death.[1] CDC also reports that among patients hospitalized for COVID-19 infection, metastatic solid tumors and any malignant neoplasm were 57% and 27% more likely to result in death, respectively.

Given the increased risk for severe disease and death from COVID-19, patients with these conditions have been strongly encouraged to diligently practice social distancing and other infection prevention activities to avoid contact with the SARS-CoV-2 virus as community transmission continues to occur. The introduction of effective and safe vaccines in December of 2020 began the effort to reduce susceptibility and community viral pressure. Older adults and people with conditions at high risk for severe disease were among the first groups recommended to receive the vaccine. Despite being among the first to be offered vaccine, people with cancer or blood disorders often have transient or permanent impaired immune function associated with the nature of their disease and/or side effects associated with treatment which may make vaccine less effective in this group. Moreover, hematological malignancies (leukemia, myeloma, lymphoma) often affect the production of white blood cells and are known to impair immune response to vaccines.[2] [3]

Despite the clear need for vaccination in this group, oncology providers struggled to secure and administer vaccine to their patients. The logistics of managing the first available vaccine products (Pfizer-BioNtech, Moderna mRNA-1273) were prohibitive for many oncology practices in Pennsylvania. Ultra-cold storage and large volume for minimal orders were two main reasons several practices were not able to become vaccine providers initially for their healthcare staff and high-risk patients. Because of this, many oncology practices advised their patients to seek vaccine as soon as they could from large health systems or government run vaccination clinics. This led to many patients on active treatment receiving their vaccine series independent of their chemotherapeutic recovery periods. This is important as many patients may have had temporary suppressed immune function at the time they received COVID vaccine, thus reducing the benefit to protect them from infection.

As part of its ongoing commitment to track the natural progression of COVID-19 and to continue to serve and protect those most vulnerable for severe disease and death, the Pennsylvania Department of Health, Bureau of Epidemiology (BOE) continues to offer antibody testing to select populations in Pennsylvania. In February of 2021, BOE identified three fully vaccinated staff members from a long-term care facility who tested negative for SARS-CoV-2 antibodies to the spike protein. Investigation of these individuals identified an active hematological or oncological condition among all three, raising concern about vaccine efficacy among people with this type of condition.

In March of 2021, the BOE through its Serology Workgroup developed a protocol to further explore the impact of COVID-19 and SARS-CoV-2 vaccination in patients with hematological or oncological conditions. Below are the four main objectives:

1. Estimate prevalence of SARS-CoV-2 antibodies among immunocompromised persons receiving care, at 0, 3, 6, 9, and 12-month intervals to assess changes in antibody status.
2. Compare antibody responses between those with history of vaccine and those without over the 12-month serology testing intervals.
3. Estimate the prevalence of SARS-CoV-2 antibodies among a cohort of previously vaccinated and unvaccinated healthcare staff working with immune compromised patients.
4. Assess differences in behaviors and related to community transmission, exposures and prevention strategies between people with antibodies to SARS-CoV-2 and those without among vaccinated and unvaccinated persons.

A full protocol for recruitment, attaining consent, sample collection, laboratory analyses, and questionnaire data collection and management was developed and received approval from the Pennsylvania Department of Health Institutional Review Board (IRB). In addition, the Serology Workgroup also engaged the Centers for Disease Control and Prevention (CDC) serology task force through the Region 3 Liaison Officer of the COVID-19 Emergency Response group to review existing literature and help refine the objectives considerate of other similar studies. Oncology research experts were also engaged at the University of Pittsburgh Medical Center to advise study methods and data interpretation.

Summary of Findings

Data was collected from three separate blood collection activities in Pennsylvania that recruited 552 total hematology/oncology patients across two sites which occurred in May, August and September of 2021. Approximately 29% of these patients (n=12) who contracted COVID-19 infection reported that they were hospitalized for their illness – a reminder that patients with a blood disorder or cancer are at high risk for severe disease requiring ongoing targeted prevention. This study also provided an estimate of the seroprevalence of SARS-CoV-2 infection among this older, health-specialized population by detecting antibodies among people who were unvaccinated. Seroprevalence estimates among unvaccinated patients increased from each collection period from 25% in May, 28% in August and 39% in September. Caution should be applied when interpreting this finding as the combined number of people for this estimate was small (N = 39), and other factors may not be accounted for including regional differences between site locations.

As the number of days since vaccine primary series increased among patients across the three collection periods (median of 58 days during the May collection period, 139 days during the August collection period, and 173 days during the September collection period), the antibody positivity decreased (88.3% during the May collection period, 83.7% during the August collection period, and 79.7% during the September collection period). Explanations for these findings may include natural waning of antibodies, but also could be confounded by

differences in disease type and severity, history of previous infection, vaccine product, and other factors between the groups. Prior to booster vaccinations, this estimate of 20% antibody negativity among these patients may warrant additional doses of vaccine and infection prevention precautions while COVID-19 continues to circulate.

Fully vaccinated patients with a hematologic malignancy (lymphoma, leukemia, myeloma, etc.) had the lowest proportion of positive antibody tests (67.6%, from all patients combined across collection periods) compared to patients with solid cancers (93.9%), hematology conditions (93.6%), and other immune suppressive conditions (78.6%). These findings are consistent with other reports and understandable given the nature of blood cancers.[4] [5] Continued diligence for infection prevention and administration of booster doses of vaccine when indicated are very important for these often-immune compromised patients.

Among fully vaccinated individuals who did not receive a 3rd vaccine dose (N=455), recipients of the Moderna vaccine had the highest proportion of positive antibody tests (91.2%), compared to 83.0% of patients who received Pfizer, and 58.3% for those who received Johnson & Johnson vaccine. The median number of days from series completion to specimen collection date was longest for Moderna vaccine recipients (153 days) compared to Pfizer (139 days) and Johnson & Johnson (131 days), suggesting that length of time since receiving vaccine does not explain the higher proportion of positive antibody tests among Moderna vaccine recipients. Though other factors may be confounding these observations, these findings are consistent with other data and suggest Moderna vaccine may be best among the current authorized vaccines in producing a serological immune response among oncology patients.[6] [7] The Johnson & Johnson product yielded subpar performance in comparison with other authorized products and careful consideration should be given before this product is used in this population if the other vaccines are available.

While most patients involved in this study were fully vaccinated, a few had received an additional dose. At the blood collection activity in September, 40 patients had received an additional dose of vaccine beyond the initial vaccine series with a median of 20 days prior to having their blood collected for antibody testing. The proportion of seropositivity among these patients (92.5%) was higher than those fully vaccinated patients who did not receive a third dose (81.4%). Three patients (7.5%) tested negative after sufficient time elapsed from receiving a 3rd dose of vaccine. Though small estimates, these data suggest that additional doses of vaccine are of benefit to cancer patients but may not improve immunity for a small subset of patients.

Our study also detected a decreasing trend among patients from the May to September collection period with respect to always wearing a mask and maintaining 6 feet of social distance when outside of the home. Estimates for always masking decreased from 95.3% in May, to 85.6% in August, to 76.7% in September. Estimates also decreased for those always maintaining 6 feet of separation from others (64.2% in May, 58.3% in August, 40.7% in September). These findings may be due in part to changes in social distancing recommendations as the state was still experiencing many cases in the Spring but went through a low level of case reports in early Summer 2021. Additional doses of vaccines administered, and pandemic fatigue may also be contributing factors to these observations.

As shown through antibody testing for SARS-CoV-2, people with immune compromising conditions including cancer and blood disorders are at increased risk for severe disease and death from COVID-19 and benefit less from the protective effect of COVID-19 vaccine compared to the general population. Because of this they should receive continued monitoring and guidance on timing and optimal products for additional vaccine doses. Community prevention activities including mask wearing, hand hygiene, social distancing, and avoidance of large crowds as COVID-19 continues to circulate should continue as public interest in these prevention strategies decreases.

Methods

Recruitment of Practices

BOE leveraged an existing relationship with a busy oncology practice in Northeastern Pennsylvania to describe the study and explore potential collaboration. BOE, Infection Control and Outbreak Response (ICOR) staff had recently provided guidance regarding management of a positive COVID-19 case among their staff and so they were receptive to hearing a proposal for antibody testing. Additional outreach was conducted to specific large practices in counties that did not have a local health department. Two practices agreed to offer the testing to their patients and staff: one in the Northeast (Practice A), and one in the Southeast (Practice B). A medical professional from each practice signed and submitted the medical standing order for the antibody test and each institution created a user account in the Bureau of Laboratories (BOL) Lab Web Portal (LWP) to order tests and receive results.

Participant Recruitment and Consent

In conjunction with the practices, BOE selected a week for the blood collection activity. All patients with a previously scheduled appointment received a letter in the mail from the practice inviting them to participate in the antibody testing opportunity. All patients regardless of vaccination status or previous infection were invited to participate. Invitations included a QR (Quick Response) code that linked to an online questionnaire through Microsoft™ Forms where people could self-register for the antibody test 2-3 weeks before the scheduled blood collection activities. Phone numbers were also included in the invitations so that patients without a smartphone could call and register for the test. Registered patients and staff received instructions on blood collection clinic details over email and flyers were posted in staff breakrooms to promote awareness. Participant consent forms were issued and signed on-site prior to study enrollment. These forms gave permission for the study coordinators to receive medical problem lists from the practice so that immune suppressive condition could be identified and matched to the antibody test results. In addition to collecting consent to participate in the study, these forms also collected participant contact information, date of birth, gender, and race/ethnicity. Consent forms and study protocols were approved by the Department's IRB.

Data Collection, Sample Collection and Results Management

During the blood collection days, BOE staff were positioned in the entry way of the practice offices. Once consent was completed and participants were enrolled in the study, staff collected information about participants' COVID-19 vaccine history (dates of dose(s), and product) by asking to see their vaccination card or by self-report. These data were recorded by research staff on paper and were later entered into an Excel document. After vaccine history was attained, paper-based questionnaires were given to patients to complete if forms were being used that captured information on previous infection and exposures, frequency of prevention activities and attitudes towards vaccine. BOE staff entered paper-based responses into an electronic Microsoft form. Busier practices relied on the use of an electronic questionnaire issued to patients and staff directly over email after the blood collection activity.

Patients with an already scheduled blood draw were given a laboratory requisition slip to present to the phlebotomist and the tube for the antibody test was added to the set of tubes for blood collection. This step avoided an extra needle stick for patients when they decided to have the antibody test before being seen by their provider. Nurses of the practice drew the blood from all patients that had an existing semi-permanent catheter. BOE staff or skilled phlebotomists from General Health Resources were onsite to collect blood from all staff and any patients who did not have a scheduled blood draw or who decided to participate after they had their blood collected for routine purposes. All samples were centrifuged within 2 hours of collection on site, refrigerated, and delivered to BOL within 40 hours after collection. Samples were processed using the EUROIMMUN Anti-SARS-CoV-2 enzyme-linked immunosorbent assay (ELISA) to detect IgG antibodies to spike protein (not a quantitative test).

Results of the antibody tests (i.e., positive, negative, or borderline) were distributed over secure email to all participants with an updated fact sheet and an invitation to speak to the COVID-19 Medical Epidemiologist over defined office hours if there were questions about how to interpret their results. All patients received a letter with their results in the mail to ensure that those who did not give an email received their results. Individuals who were unable to access their results were referred by practice administration or they reached out directly to the dedicated resource account for this study. Individual results were downloaded from the LWP for all patients and securely provided to the practice for inclusion in the patient electronic medical records. Finally, a link to an online 30-item questionnaire (hosted on Microsoft™ Forms) was also distributed to all staff within the secure email results communication. This questionnaire collected information on behaviors, perceptions, and attitudes that may impact risk of contracting COVID-19. Reminder emails were sent two weeks later to encourage more participants to complete the questionnaire.

Medical problem lists for all patients were received securely either over encrypted email or paper copies provided by the practice administration. Problem lists were used to assign all patients into clinical categories. These included hematology or oncology main classifications. Oncology patients were further labeled as hematologic malignancy patients or solid cancer patients. Patients with a hematological malignancy were further subclassified as either having leukemia, lymphoma, myeloma, myelodysplastic syndrome or other condition.

Statistical Analysis

Questionnaire data, laboratory data, and participant registration data were merged, cleaned, and analyzed using SAS Enterprise Guide, version 7.1 (SAS Institute Inc., Cary, NC, USA). Summary tables were developed to present data on participant demographics, questionnaire response data, and serology results by participant vaccination status, vaccine product received, whether they received a third vaccine dose and patient condition category. To summarize vaccine data, fully vaccinated patients were defined as patients who submitted samples at least 14 days after completing a full vaccine series (i.e., both doses of a 2-dose series or a single dose of a one dose vaccine). Partially vaccinated patients were those who received at least one vaccine dose but did not meet the fully vaccinated definition. Unvaccinated participants did not receive any COVID-19 vaccine. For all summary tables

presented, patients are grouped under the collection period during which they submitted their first (or only) sample. This was done so the patients described under each collection period are a unique sample; no patient is counted twice in any of the summary tables.

Differences in demographic characteristics of patients recruited in each collection period were assessed using chi-square or Fisher's exact tests for categorical variables and Kruskal-Wallis tests for continuous variables. Fisher's exact tests were also used to determine whether there were significant differences in fully vaccinated patients' likelihood of testing positive for SARS-CoV-2 antibodies by the vaccine product they received and by their condition category. For these analyses patients who were negative or borderline were recoded into one group to compare those who tested positive to those who did not.

Due to observed differences in serology results among fully vaccinated patients by condition category, site-specific univariate logistic regression models were developed to assess differences in serology results among fully vaccinated patients by condition category. These models assessed differences across the three condition categories that included at least 3 patients from each collection period (i.e., hematology, solid cancer, and hematologic malignancy). The hematology patient category was used as the reference category for these models, as these patients were not known to have had a condition that may have impacted their immune function at the time of vaccination. Finally, descriptions of patients who submitted serology samples more than once (i.e., during different collection periods at the same site) and had a change in their serology results across collection periods are included.

Findings

Demographics by Study Site

There were three separate blood collection activities at two distinct sites that recruited 552 unique patients. Each collection period occurred over a five-day period (Monday - Friday) in May 2021, August 2021, and September 2021. The May and August collection occurred at Practice A and the September collection occurred at Practice B. Some patients at practice A submitted specimens during both collection periods. In order to compare patient samples recruited during each collection period, patients are assigned to the collection period during which they submitted their first (or only) sample. This applies to all summary tables below.

Demographics, antibody results, vaccination status and medical conditions of patients are summarized by site and collection period in Table 1. Across all collection periods, patient age ranged from 20-90 years (at Practice A median age was 69 in May and 67 in August, at Practice B median age was 66 in September). In addition, across all collection periods, most patients were white (>97. 0% of patients), non-Hispanic (>95.0% of patients in all collection periods), and female (>67.0% of patients in all collection periods). Self-reported questionnaires were completed by 77.2% of patients where history of previous infection was captured. Because this was not completed for each participant, previous history of infection was not included in the analysis and therefore it is not known if antibodies due to previous infection contribute to positive antibody test results among fully vaccinated patients.

At the time of sample collection, most patients were fully vaccinated (87.0% in May, 90.3% in August, and 92.5% in September) and positive for SARS-CoV-2 antibodies (88.3% in May, 83.7% in August, and 79.7% in September). Across all collection periods, the most common vaccine received by patients was the Moderna vaccine (received by more than half of patients across all collection periods), followed by the Pfizer vaccine, then Johnson & Johnson. The most common patient condition category was solid cancer (including 51.3% of patients in May, 48.5% of patients in August, and 59.4% in September). At Practice A, the second most common condition category was hematology (31.2% in May and 34.2% in August) followed by hematologic malignancy (16.2% in May and 16.3% in August). At Practice B, the second most common patient category was hematologic malignancy (28.6%) followed by “other” types of oncology-related conditions (5.9%).

Although the proportion of patients who were fully vaccinated increased over time (87.0% in May 2021, 90.3% in August 2021, and 92.5% in September 2021), the proportion of patients who tested positive for SARS-CoV-2 antibodies decreased (88.3% in May 2021, 83.7% in August 2021, and 79.7% in September 2021). This may be due in part to patients reporting that a longer time had passed since receiving their last vaccine dose (the median number of days since patients received their second dose [or only dose if they received Johnson & Johnson] was 58 in May 2021, 139 in August 2021, and 173 in September 2021). However, this trend may also be impacted by differences in patients’ condition, age, vaccine product, previous infection with COVID-19, or other variables that may impact antibody test results.

Table 1. Demographics Among Patients by Site and First Sample Date

	Practice A		Practice B	Total	p-value[1]
Collection Dates	5/3/2021-5/7/2021	8/2/2021-8/6/2021	9/13/2021-9/17/2021	5/3/2021-9/17/2021	NA
Total Samples Collected	154	196	202	552	NA
Age Median (Range)	69 (38-88)	67 (20-90)	66 (27-89)	66 (20-90)	
Race N (%)					0.76
White	147 (98.0%)[2]	171 (97.7%)[4]	196 (97.5%)[8]	514 (97.7%)[11]	
Black	1 (0.7%)[2]	1 (0.6%)[4]	2 (1.0%)[8]	4 (0.8%)[11]	
Asian	0 (0.0%)[2]	1 (0.6%)[4]	2 (1.0%)[8]	3 (0.6%)[11]	
Other	2 (1.4%)[2]	2 (1.1%)[4]	1 (0.5%)[8]	5 (0.9%)[11]	
Ethnicity N (%)					0.19
Hispanic	0 (0.0%)[3]	3 (3.0%)[5]	2 (1.6%)[9]	5 (1.4%)[12]	
Not Hispanic	124 (99.2%)[3]	97 (96.0%)[5]	122 (95.3%)[9]	343 (96.9%)[12]	
Unknown	1 (0.80%)[3]	1 (1.0%)[5]	4 (3.1%)[9]	6 (1.7%)[12]	
Gender N (%)					0.70
Female	104 (67.5%)	127 (71.8%)[6]	142 (70.3%)	373 (70.0%)[6]	
Male	50 (32.5%)	50 (28.3%)[6]	60 (29.7%)	160 (30.0%)[6]	
Patient Condition Category N (%)					<0.01
Hematology	48 (31.2%)	67 (34.2%)	9 (4.5%)	124 (22.5%)	
Rheumatology	0 (0.0%)	0 (0.0%)	3 (1.5%)	3 (0.5%)	
Oncology: Solid Cancer	79 (51.3%)	95 (48.5%)	120 (59.4%)	294 (53.3%)	
Oncology: Hematologic Malignancy	25 (16.2%)	32 (16.3%)	58 (28.7%)	115 (20.8%)	
Oncology: Other	2 (1.3%)	2 (1.0%)	12 (5.9%)	16 (2.9%)	
Days Since Vaccine (Fully Vaccinated Only) Median (Range)	58 (13-95)	139 (36-187)	173 (16-246)	149 (13-246)	
Vaccination Status N (%)					<0.01
Fully Vaccinated	134 (87.0%)	176 (90.3%)	185 (92.5%)[10]	495 (90.2%)[10]	
Partially Vaccinated	12 (7.8%)	1 (0.5%)	2 (1.0%)[10]	15 (2.7%)[10]	
Not Vaccinated	8 (5.2%)	18 (9.2%)	13 (6.5%)[10]	39 (7.1%)[10]	
Vaccine Product Received N (%)					<0.01
Pfizer	41 (28.1%)	59 (33.9%)[7]	74 (40.0%)	174 (34.5%)[7]	
Moderna	103 (70.6%)	106 (60.9%)[7]	109 (58.9%)	318 (63.0%)[7]	
Johnson & Johnson	2 (1.4%)	9 (5.2%)[7]	1 (0.5%)	12 (2.4%)[7]	
Other/Mix	0 (0.0%)	0 (0.0%)[7]	1 (0.5%)	1 (0.2%)[7]	
Serology Results N (%)					0.18
Positive	136 (88.3%)	164 (83.7%)	161 (79.7%)	461 (83.5%)	
Negative	17 (11.0%)	27 (13.8%)	38 (18.8%)	82 (14.9%)	
Borderline	1 (0.7%)	5 (2.5%)	3 (1.5%)	9 (1.6%)	

[1]P-values were calculated using Chi-Square or Fisher Exact tests (when at least one group contained less than N=5) for categorical variables and using Kruskal-Wallis tests for continuous variables (i.e., age) to compare differences across sites; [2]Missing for N=4; [3]Missing for N=29; [4]Missing for N=21; [5]Missing for N=95; [6]Missing for N=19; [7]Missing for N=22; [8]Missing for N=1; [9]Missing for N=74; [10]Missing for N=2; [11]Missing for N=26; [12]Missing for N=198

Serology and Vaccination Data by Study Site

In Table 2, patients' serology results are summarized by their vaccination status at the time samples were collected. Importantly, data in Tables 2-4 do not account for impact of previous infection and exclude patients who received a third dose of vaccine to improve comparability across collection periods.

Among fully vaccinated patients, 91.8% tested positive for antibodies in May, 89.2% in August, and 81.4% in September. Among partially vaccinated patients, 91.7% tested positive for antibodies in May, 100% in August, and 50.0% in September. Finally, among unvaccinated patients, 25.0% tested positive for antibodies in May, 27.8% in August, and 38.5% in September. Across the three collection periods, a total of 48 fully vaccinated patients (10.5%) tested negative for SARS-CoV-2 antibodies. Among these 48 patients, 36 (75.0%) completed questionnaires, none reported a previous COVID-19 diagnosis and 3 (8.3%) reported being a COVID-19 close contact on their questionnaire.

Each collection period identified unvaccinated patients who tested positive for antibodies therefore representing those who were previously infected. In total,12 of 39 (30.8%) unvaccinated patients tested positive for SARS-CoV-2 antibodies. Out of the 11 of these patients who completed questionnaires, 8 (72.7%) reported previously being diagnosed with COVID-19, 2 (18.2%) reported being hospitalized for COVID-19, and 6 (54.5%) reported being a close contact of someone who was diagnosed with COVID-19 (other questionnaire data is summarized in Table 6).

Table 2. Serology Results among Hematology/Oncology Patients by Vaccination Status and Site[1]

Practice A				
May 2021 Visit (5/3/2021-5/7/2021)				
	Positive	Negative	Borderline	Total
Fully Vaccinated	123 (91.8%)	10 (7.5%)	1 (0.8%)	134
Partially Vaccinated	11 (91.7%)	1 (8.3%)	0 (0.0%)	12
Not Vaccinated	2 (25.0%)	6 (75.0%)	0 (0.0%)	8
August 2021 Visit (8/2/2021-8/6/2021)[2]				
	Positive	Negative	Borderline	Total
Fully Vaccinated	157 (89.2%)	14 (8.0%)	5 (2.8%)	176
Partially Vaccinated	1 (100%)	0 (0.0%)	0 (0.0%)	1
Not Vaccinated	5 (27.8%)	13 (72.2%)	0 (0.0%)	18
Practice B				
September 2021 Visit (9/13/2021-9/17/2021)[3]				
	Positive	Negative	Borderline	Total
Fully Vaccinated	118 (81.4%)	24 (16.6%)	3 (2.1%)	145
Partially Vaccinated	1 (50.0%)	1 (50.0%)	0 (0.0%)	2
Not Vaccinated	5 (38.5%)	8 (61.5%)	0 (0.0%)	13

[1]Excludes patients who received a third dose of vaccine; [2]Missing for N=1; [3]Missing for N=2

Table 3 summarizes serology results among fully vaccinated patients by collection period and the vaccine product they received. In addition, the number of days since patients received their most recent COVID-19 vaccine dose is included in Table 3 for comparison purposes. Among fully vaccinated patients who received the Pfizer vaccine, 94.6% in May at Practice A, 84.5% in August at Practice A, and 74.1% in September at Practice B tested positive for SARS-CoV-2 antibodies. Among those who received the Moderna vaccine, 91.6% in May at Practice A, 94.3% in August at Practice A, and 86.9% in September at Practice B tested positive for SARS-CoV-2 antibodies. Among those who received the Johnson & Johnson vaccine 50.0% in May at Practice A, 55.6% in August at Practice A, and 100% in September at Practice B were positive for antibodies (please note that at the site where 100% of Johnson & Johnson vaccine recipients were positive for antibodies, only 1 patient received the vaccine).

One patient at Practice B received a single dose of the Moderna vaccine and had a slight allergic reaction. For this reason, rather than receiving another Moderna vaccine dose, this patient later received a single dose of the Johnson & Johnson vaccine. For the purposes of this analysis, this patient was considered fully vaccinated and tested negative for SARS-CoV-2 antibodies (Table 3).

Fisher's exact tests were used to determine whether there were significant differences in patients' likelihood of testing positive for SARS-CoV-2 antibodies by vaccine product received. At the May 2021 visit and Practice A, there were no significant differences observed ($p=0.18$), however significant differences were observed during the August 2021 visit at Practice A, at Practice B, and across all three sites combined ($p<0.05$).

Table 3. Serology Results among Hematology/Oncology Patients Who Received Two Doses of Vaccine by Vaccine Product and Site[1]

Practice A					
May 2021 Visit (5/3/2021-5/7/2021)					
	Days Since Vaccine Median (Range)	Positive	Negative	Borderline	Total
Pfizer	38 (15-85)	35 (94.6%)	2 (5.4%)	0 (0.0%)	37
Moderna	61 (14-95)	87 (91.6%)	7 (7.4%)	1 (1.1%)	95
Johnson & Johnson	38 (25-50)	1 (50.0%)	1 (50.0%)	0 (0.0%)	2
August 2021 Visit (8/2/2021-8/6/2021)[2]					
	Days Since Vaccine Median (Range)	Positive	Negative	Borderline	Total
Pfizer	124 (49-187)	49 (84.5%)	7 (12.1%)	2 (3.5%)	58
Moderna	152 (26-182)	100 (94.3%)	5 (4.7%)	1 (0.9%)	106
Johnson & Johnson	124 (89-143)	5 (55.6%)	2 (22.2%)	2 (22.2%)	9
Practice B					
September 2021 Visit (9/13/2021-9/17/2021)[3]					
	Days Since Vaccine Median (Range)	Positive	Negative	Borderline	Total
Pfizer	161 (16-246)	43 (74.1%)	14 (24.1%)	1 (1.7%)	58
Moderna	186 (24-240)	73 (86.9%)	9 (10.7%)	2 (2.4%)	84
Johnson & Johnson	183	1 (100%)	0 (0.0%)	0 (0.0%)	1
Moderna and Johnson & Johnson	54	0 (0.0%)	1 (100%)	0 (0.0%)	1
Combined Data[4]					
	Days Since Vaccine Median (Range)	Positive	Negative	Borderline	Total
Pfizer	139 (15-246)	127 (83.0%)	23 (15.0%)	3 (2.0%)	153
Moderna	153 (14-240)	260 (91.2%)	21 (7.4%)	4 (1.4%)	285
Johnson & Johnson	131 (25-183)	7 (58.3%)	3 (25.0%)	2 (16.7%)	12
Moderna and Johnson & Johnson	54	0 (0.0%)	1 (100%)	0 (0.0%)	1

[1]Excludes patients who received a third dose of vaccine; [2]Missing for N=3; [3]Missing for N=1; [4]Missing for N=4

Table 4 summarizes serology results among fully vaccinated patients by collection period and condition category. As above, this table also summarizes the number of days since patients received their most recent COVID-19 vaccine dose for comparison purposes. The proportion of fully vaccinated patients who tested negative for SARS-CoV-2 antibodies were compared across condition categories that included at least 3 patients from each collection period (i.e., hematology, solid cancer, and hematologic malignancy). Overall, a smaller proportion of fully vaccinated patients with a hematologic malignancy tested positive for SARS-CoV-2 antibodies (65.2% in May at Practice A, 68.8% in August at Practice A, and 68.3% in September at Practice B) than patients with solid cancer (97.1% in May at Practice A, 94.1% in August at Practice A, and 93.3% in September at Practice B) or hematology patients (97.6% in May at Practice A, 93.1% in August at Practice A, and 77.8% in September at Practice B).

Table 5 further summarizes serology results among fully vaccinated hematologic malignancy patients by their type of hematologic malignancy. Among this group of 94 individuals, lymphoma patients had the lowest proportion that were positive for antibodies (58.1%) followed by patients with leukemia (66.7%). Fisher's exact tests found no significant differences in serology results by hematologic malignancy types (p=0.60).

At Practice A during the May 2021 collection period, hematologic malignancy patients had 21.9 times the odds of testing negative or borderline for SARS-CoV-2 antibodies than hematology patients (unadjusted models, 95% CI: 2.5-189.9). However, the likelihood of testing negative or borderline for SARS-CoV-2 antibodies was not significantly different between fully vaccinated solid cancer patients and hematology patients (unadjusted OR= 1.2, 95% CI: 0.1-14.1). Similar findings were observed at Practice A during the August 2021 collection period. At that time, hematologic malignancy patients had 6.1 times the odds of testing negative or borderline for SARS-CoV-2 antibodies than hematology patients (95% CI: 1.7-21.7), and no significant differences were found between fully vaccinated solid cancer patients and hematology patients (unadjusted OR= 0.8, 95% CI: 0.2-3.3). At Practice B, during the September 2021 collection period, no significant differences were found between fully vaccinated hematologic malignancy patients and hematology patients (unadjusted OR= 1.6, 95% CI: 0.3-8.9) or between fully vaccinated solid cancer patients and hematology patients (unadjusted OR= 0.4, 95% CI: 0.08-2.3).

Table 4. Serology Results among Fully Vaccinated Hematology/Oncology Patients by Condition Category and Site[1]

Practice A				
May 2021 Visit (5/3/2021-5/7/2021)				
	Hematology	Other[3]	Oncology	
			Solid Cancer	Hematologic Malignancy
Days since vaccine[2]	57 (14-92)	130	58 (14-95)	58 (17-80)
Positive	41 (97.6%)	1 (100%)	66 (97.1%)	15 (65.2%)
Negative	1 (2.4%)	0 (0.0%)	2 (2.9%)	7 (31.8%)
Borderline	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.6%)
August 2021 Visit (8/2/2021-8/6/2021)				
	Hematology	Other[3]	Oncology	
			Solid Cancer	Hematologic Malignancy
Days since vaccine[2]	129 (36-182)	139	138 (49-187)	145 (103-180)
Positive	54 (93.1%)	1 (100%)	80 (94.1%)	22 (68.8%)
Negative	2 (3.5%)	0 (0.0%)	3 (3.5%)	9 (28.1%)
Borderline	2 (3.5%)	0 (0.0%)	2 (2.4%)	1 (3.1%)
Practice B				
September 2021 Visit (9/13/2021-9/17/2021)[2]				
	Hematology	Other[3]	Oncology	
			Solid Cancer	Hematologic Malignancy
Days since vaccine[1,2]	187 (94-216)	178 (148-239)	171 (46-246)	177 (16-225)
Positive	7 (77.8%)	8 (72.7%)	75 (89.3%)	28 (68.3%)
Negative	2 (22.2%)	3 (27.3%)	6 (7.1%)	13 (31.7%)
Borderline	0 (0.0%)	0 (0.0%)	3 (3.6%)	0 (0.0%)
Combined				
	Hematology	Other[3]	Oncology	
			Solid Cancer	Hematologic Malignancy
Days since vaccine[1,2]	129 (14-216)	175 (130-239)	149 (14-246)	152.5 (16-225)
Positive	102 (93.6%)	10 (78.6%)	221 (93.3%)	65 (67.7%)
Negative	5 (4.6%)	3 (21.4%)	11 (4.6%)	29 (30.2%)
Borderline	2 (1.8%)	0 (0.0%)	5 (2.1%)	2 (2.1%)

[1]Excludes patients who received a third dose of vaccine; [2]Median (Range); [3]Includes immune disorders, rheumatology patients, and other conditions.

Table 5. Serology Results among Fully Vaccinated Hematologic Malignancy Patient by Disease Type[1]

	Leukemia	Lymphoma	Myeloma	Myelodysplastic Syndrome	Total
Positive	24 (66.7%)	18 (58.1%)	16 (76.2%)	5 (83.3%)	63 (67.0%)
Negative	12 (33.3%)	12 (38.7%)	4 (19.1%)	1 (16.7%)	29 (30.1%)
Borderline	0 (0.0%)	1 (3.2%)	1 (4.8%)	0 (0.0%)	2 (2.1%)
Total	36	31	21	6	94

[1]Missing for N=2

Third doses of vaccines became increasingly available to patients with immune compromising conditions in Pennsylvania. For this reason, while no patients received third doses of vaccine at Practice A, 40 patients (21.6%) at Practice B received a third vaccine dose prior to submitting a sample. Serology results by whether or not patients receive a third dose are summarized in Table 6 for Practice B patients only. Out of the 40 patients who received a third dose, 92.5% tested positive for SARS-CoV-2 antibodies and 3 (7.5%) tested negative. The median number of days since third dose was 20, suggesting that most of these patients would have developed antibodies from the vaccine if able. Even so, 3 patients (7.5%) did not seroconvert after a third dose of vaccine though enough time had passed since receiving third dose and having their blood collected (19, 21, and 25 days). Future analyses will further explore the impact of third vaccine doses on this patient population.

Table 6. Serology Results among Practice B Patients by whether they Received a Third Dose of Vaccine

September 2021 Visit (9/13/2021-9/17/2021)[2]					
	Days Since Vaccine Median (Range)	Positive	Negative	Borderline	Total
Received a 3rd Dose	20 (1-31)	37 (92.5%)	3 (7.5%)	0 (0.0%)	40
Did not Receive a 3rd Dose	173 (16-246)	118 (81.4%)	24 (16.6%)	3 (2.1%)	145

Questionnaire Data Summary

Table 7 summarizes questionnaire data collected from patients who submitted samples at Practice A and Practice B. A total of 426 questionnaires were collected among the 552 patients for analysis (77.2% completion rate). Across the three collection periods, 42 patients reported a previous COVID-19 diagnosis. Among these patients, 12 were ever hospitalized for COVID-19. A total of 54 patients reported being a close contact of someone who was diagnosed with COVID-19 prior to submitting their sample.

Most patients reported leaving their home at least 2 times per week (>78.0% in each collection period) and reported that they “always” wear masks outside of their home (>73.0% in each collection period). In addition, most patients at Practice A reported that they “always”

maintain social distance outside of their home (95.3% in May and 85.6% in August) while most patients at Practice B reported that they “sometimes” maintain social distance outside of their home (60.2%). Most patients wash their hands at least 5 times per day (>75.0% in each collection period) and over one-third of patients in each collection period know someone who has died from COVID-19.

Notably, trends in Table 6 show that the proportion of patients who report “always” masking or social distancing outside of their home has decreased over time. While this does not account for other variables that may impact this relationship, this finding may demonstrate changes in patient behavior as vaccine is received, social distancing is relaxed or as third doses become available.

Table 7. Hematology/Oncology Patients Questionnaire Data by Site

	Practice A		Practice B	Total
	5/3/2021-5/7/2021	8/2/2021-8/6/2021	9/13/2021-9/17/2021	5/3/2021-9/17/2021
Total Questionnaires Collected	153	160	113	426
Previous known COVID-19 Diagnosis N (%)[1]	14 (9.2%)[1]	17 (10.7%)[1]	12 (10.6%)	43 (10.1%)[10]
Previously Hospitalized for COVID-19 N (%)[2]	3 (21.4%)[2]	6 (35.2%)[2]	3 (27.2%)[2]	12 (27.9%)
Ever was a close contact of someone with COVID-19 N (%)[3]	23 (15.3%)[3]	17 (10.6%)	15 (13.3%)	55 (13.0%)[3]
Frequency leaving home per week N (%)				
Never	3 (2.0%)[4]	4 (2.6%)[6]	1 (0.9%)[1]	8 (1.9%)[11]
1 time	25 (16.9%)[4]	29 (18.8%)[6]	18 (16.1%)[1]	72 (17.4%)[11]
2 to 4 times	56 (37.8%)[4]	64 (41.6%)[6]	51 (45.5%)[1]	171 (41.3%)[11]
More than 4 times	64 (43.2%)[4]	57 (37.0%)[6]	42 (37.5%)[1]	163 (39.4%)[11]
Most frequently reported reasons for leaving home				
Medical Appointments	133 (86.9%)	122 (76.3%)	99 (87.6%)	354 (83.1%)
Grocery Shopping	115 (75.2%)	116 (72.5%)	85 (75.2%)	316 (74.2%)
Shopping for other necessities	79 (51.6%)	74 (46.3%)	62 (54.9%)	215 (50.5%)
Frequency of Masking Wearing Outside of Home N (%)				
Always	143 (95.3%)[3]	131 (85.6%)[7]	86 (76.7%)[1]	360 (86.8%)[12]
Sometimes	7 (4.7%)[3]	21 (13.7%)[7]	21 (18.8%)[1]	49 (11.8%)[12]
Rarely	0 (0.0%)[3]	1 (0.7%)[7]	5 (4.5%)[1]	6 (1.5%)[12]
Never	0 (0.0%)[3]	0 (0.0%)[7]	0 (0.0%)[1]	0 (0.0%)[12]
Frequency of Social Distancing Outside of Home N (%)				
Always	95 (64.2%)[4]	88 (58.3%)[8]	46 (40.7%)	229 (55.6%)[13]
Sometimes	52 (35.1%)[4]	62 (41.1%)[8]	62 (54.9%)	176 (42.7%)[13]
Rarely	1 (0.7%)[4]	1 (0.7%)[8]	5 (4.4)	7 (1.7%)[13]
Never	0 (0.0%)[4]	0 (0.0%)[8]	0 (0.0%)	0 (0.0%)[13]
Frequency of Handwashing per Day N (%)				
Never	0 (0.0%)[3]	1 (0.7%)[7]	0 (0.0%)	1 (0.2%)[9]
1-4 times	24 (16.0%)[3]	20 (13.1%)[7]	29 (25.7%)	73 (17.6%)[9]
5-10 times	73 (48.7%)[3]	75 (49.0%)[7]	52 (46.0%)	200 (48.1%)[9]
More than 10 times	53 (35.3%)[3]	57 (37.3%)[7]	32 (28.3%)	142 (34.1%)[9]
Knows someone who has died of COVID-19 N (%)	57 (38.3%)[5]	56 (37.3%)[9]	43 (38.4%)[1]	156 (38.0%)[14]

[1]Missing for N=1; [2]Percentage is among those who were diagnosed with COVID-19; [3]Missing for N=3; [4]Missing for N=5; [5]Missing for N=4; [6]Missing for N=6; [7]Missing for N=7; [8]Missing for N=9; [9]Missing for N=10; [10]Missing for N=2; [11]Missing for N=12; [12]Missing for N=11; [13]Missing for N=14; [14]Missing for N=15

Redraw Serology Data Summary

In addition to the 196 patients who submitted their first sample during the second (August 2021) visit to Practice A, there were 74 patients who submitted a sample during both the May and August visit. Of these, the majority N=70 (94.6%), had the same result during both the May and August visit (65 were positive for SARS-CoV-2 antibodies in May and were also positive in August and 5 were negative for SARS-CoV-2 antibodies in May and were also negative in August).

Of the remaining 4 who had different results during the August collection period, 2 were negative in May and became positive in August. Neither of these patients reported a previous COVID-19 infection or close contact. One was fully vaccinated during both collection periods (with Moderna) and was diagnosed with lymphoma. The other was partially vaccinated during the first collection period and was fully vaccinated during the second collection period and was a solid cancer patient.

One patient tested borderline in May and tested negative during the August collection period. This patient was a myeloma patient, was fully vaccinated in March 2021 with the Moderna vaccine, and had no reported previous COVID-19 diagnosis or close contact. Finally, one patient was positive for SARS-CoV-2 antibodies in May but then tested negative in August. This patient was a solid cancer patient who was fully vaccinated with the Moderna vaccine in April 2021. This patient also did not report a previous COVID-19 diagnosis or close contact.

Conclusions

This report analyzes findings from three separate blood collection activities in Pennsylvania that recruited 552 total hematology/oncology patients across two sites in May, August and September of 2021. Forty-two patients in this cohort identified that they had a COVID-19 infection previously and among those,12 (28.6%) reported that they were hospitalized for their COVID-19 illness. This estimate for hospitalization is high and consistent with known increased risk for severe disease among older adults and those with cancer and blood disorders.

There were 12 of 39 (30.8%) unvaccinated patients who tested positive for antibodies at the time of their blood collection indicating they had previous infection. Though small numbers and derived from a specialized older adult population, this estimate is informative and suggests that by the end of summer 2021, approximately one-third of the Pennsylvania population had contracted COVID-19. In May this finding was 25.0%, 27.8% in August, and 38.5% in September showing an increasing trend consistent with case reports over the same time period.

Age-similar, mostly vaccinated patients showed an overall decreasing trend in antibody positivity from 88.3% in May, 83.7% in August and 79.7% in September. This is likely due to the increasing number of days from full vaccination to date of blood collection among those vaccinated (median 58, 139, 173 for each blood collection period, respectively) but could also be confounded by differences in disease type and severity, vaccine product, and other factors unaccounted for. These estimates indicate potential susceptibility to COVID infection approaching 20% among patients with a condition that puts them at high risk for severe disease. Additional doses of vaccine and infection prevention precautions are warranted to maintain protection in this population.

Fully vaccinated hematologic malignancy patients had the lowest proportion of positive antibody tests for each collection period and combined (67.6%) compared to patients with solid cancers (93.9%), hematology conditions (93.6%), and other immune suppressive conditions (78.6%). The median number of days since vaccine series completion ranged from 129 – 175 days among the 4 groups (153 days for hematologic malignancy patients). These findings are consistent with other reports and understandable given the nature of blood cancers. Continued diligence for infection prevention and administration of booster doses of vaccine when indicated is very important for patients with leukemia, myeloma, lymphoma, and myelodysplastic syndrome.

Combining all data among fully vaccinated patients with a primary series, those who received the Moderna vaccine had the highest proportion of positive antibody tests (91.2%), compared to 83.0% of patients who received Pfizer, and 58.3% for those who received Johnson & Johnson vaccine. The median number of days since series completion was similar between all three products though Moderna had the longest median number of days (153) compared to Pfizer (139) and Johnson & Johnson (131). Though other factors may be confounding these observations, these findings are consistent with other data and suggest Moderna vaccine may be best among the current authorized vaccines in producing the most robust serological immune response to protect oncology patients.

At the Practice B collection in September, 40 patients had received a third dose of vaccine with a median of 20 days prior to having their blood collected for antibody testing. More of these patients tested positive for antibodies (92.5%) compared to 81.4% of other fully vaccinated patients. It is important to note that 3 patients (7.5%) tested negative after sufficient time elapsed from receiving a 3rd dose of vaccine. Though small estimates, these data suggest that additional doses of vaccine are of benefit to cancer patients but may not improve immunity for a small subset of patients.

Our study also detected a decreasing trend among patients with respect to always wearing a mask and maintaining 6 feet of social distance when outside of the home from May to September 2021. Estimates for always masking decreased from 95.3% in May, to 85.6% in August, to 76.7% in September. Estimates also deceased for those always maintaining 6 feet of separation from others (64.2% in May, 58.3% in August, 40.7% in September). These findings may be due in part to changes in social distancing recommendations as the state was still experiencing many cases in the Spring but went through a low level of case reports in early Summer. Additional doses of vaccine, and pandemic fatigue may also be contributing factors to these observations.

Citations

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