ORIGINAL RESEARCH

COVID-19 mRNA Vaccination Trends Among Immunocompromised Patients

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Introduction: **Immunocompromised patients are at increased risk of contracting severe COVID-19 infection. The purpose of this study was to assess COVID-19 vaccination trends of immunocompromised patients at a large, urban primary care setting.**

Methods: **A retrospective chart review of immunocompromised patients who had a visit between 1/1/2021 and 5/15/2022 at Thomas Jefferson University's Department of Family and Community Medicine (DFCM) was conducted. Patient charts were reviewed for demographics, number of visits to the DFCM, immunocompromising diagnoses, and COVID-19 mRNA vaccination status, including vaccination type and number of vaccine doses received. Descriptive statistics were calculated. Paired *t* tests were conducted to assess relationships between immunocompromised patients with ≥3 mRNA vaccine doses and those with ≤2 mRNA vaccine doses.**

Results: **A total of 887 patients were included. Most patients were Black (66.7%), above the age of 50 (82.1%), and male (55.9%). Solid tumor cancers (62.6%) and HIV/AIDS (23.8%) were the most represented immunocompromising diagnoses. Overall, 556 patients received ≥3 mRNA vaccine doses (62.7%) and 331 patients received ≤2 mRNA vaccine doses (37.3%). Eighty-three patients (9.4%) had no COVID-19 vaccines on record. Of the 591 Black patients, 248 (42%) received ≤2 mRNA vaccine doses.**

Conclusion: **Despite the majority of the sample receiving ≥3 mRNA vaccine doses, disparities in vaccination rates exist, especially when comparing White and Black patients. Vaccination rates in immunocompromised patients should be improved, and primary care providers should prioritize outreach efforts focusing on patient-centered COVID-19 vaccine education in these populations. (J Am Board Fam Med 2023;36:000–000.)**

Keywords: **COVID-19, COVID-19 Vaccines, Immunocompromised Patient, Retrospective Studies, Vaccination**

Introduction

Patients with compromised immune systems, either from disease-related immunodeficiency or from taking immunosuppressive medications, are among the most susceptible to COVID-19 infection. Although susceptibility varies depending on the degree of immune dysfunction or suppression, it is estimated that having a compromised immune system makes patients twice as more likely to contract a COVID-19 infection compared with an immunocompetent patient.[1] Immunocompromised patients are also at an increased risk of developing severe COVID-19 disease and hospitalization.[2] This is an area of concern to both patients and physicians, as patients with immune dysfunction need additional protection from COVID-19 compared with the general population.

Although COVID-19 mRNA vaccines, such as BNT162b2 vaccine from Pfizer-BioNTech and mRNA-1273 vaccine from Moderna, have been shown to effectively protect immunocompetent patients from COVID-19 infection and hospitalization,

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immunocompromised patients are less likely to mount a response to these COVID-19 mRNA vaccines.[3–5] Early immunogenicity and vaccine effectiveness studies suggested that immunocompromised patients had a poor response in terms of seroconversion to 2 doses of a COVID-19 mRNA vaccine. A study of solid organ transplants recipients showed that only 17% of participants had antibodies against the SARS-CoV-2 spike protein 20 days after their first dose, and only 54% of participants had detectable antibodies 29 days after receiving their second dose.[6,7] Another study of cancer patients found that after 2 doses of an mRNA vaccine, 52.7% of patients with hematologic malignancy and 8.2% with solid malignancy receiving cytopenic therapy had no seroconversion.[8] A large, retrospective cohort study of COVID-19 data highlights the clinical implications of these studies, as patients with immune dysfunction, such as human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), solid organ transplant, and rheumatoid arthritis, had a higher rate of breakthrough infection and worse outcomes even after full (2 doses) or partial (1 dose) vaccination, when compared with immunocompetent patients.[9]

Due to the variable immune response to 2 doses of an mRNA vaccine in immunocompromised patients, the United States Center for Disease Control and Prevention (CDC) upgraded their recommendation from 2 doses of an mRNA vaccine to 3 doses in August of 2021 for this population. Several studies found a third dose of an mRNA vaccine in immunocompromised patients improved immunogenicity and lowered incidence of COVID-19 infection compared with immunocompromised patients with 2 mRNA vaccine doses.[9–12] However, many patients in these studies still did not respond or had a poor immunologic response to a third dose. With inconsistent responses to COVID-19 mRNA vaccines, along with the emergence of new COVID-19 strains and waning immunity among those who were vaccinated, the CDC, for most of 2022, recommended 3 initial doses of an mRNA vaccine followed by 2 booster doses for moderately to severely immunocompromised patients.[13]

Due to the rapidly changing CDC guidelines for COVID-19 vaccination over the course of the pandemic, physicians and patients may not always be up to date with the most current COVID-19 immunization recommendations for immunocompromised patients. In order for physicians to provide proper counseling and guidance to immunocompromised patients as the COVID-19 pandemic continues, they should be aware of mRNA vaccination trends among this population. The purpose of this study was to conduct a retrospective chart review to assess the COVID-19 vaccination statuses of immunocompromised patients at a large, urban primary care setting in Philadelphia, Pennsylvania.

Methods

This study was a retrospective cohort study of patients with immunocompromising diagnoses seen by providers at Thomas Jefferson University's Department of Family and Community Medicine (DFCM) in Philadelphia, Pennsylvania. This study was determined to be exempt from review by the Thomas Jefferson University Institutional Review Board (#22E.448).

Process and Sample Establishment

Immunocompromising diagnoses of interest were adapted from previously published literature and were organized into 6 categories: hematologic cancers, solid tumor cancers, autoimmune disorders, solid organ transplant recipients, HIV/AIDS, and patients on dialysis.[14,15] A report of patients from DFCM with at least 1 immunocompromising diagnosis of interest was generated using the electronic medical records (EMR) system.

Patients were excluded from the study if they did not have at least 1 visit with a DFCM provider in the time frame between 01/01/2021 and 05/01/2022. Patients were also excluded if, on chart review, they were mislabeled as having an immunocompromising diagnosis of interest or had a confidential, locked record. Lastly, patients were excluded if they received a non-mRNA vaccine at any time during the study period or as a primary dose (eg, receiving the JNJ-78436735 viral vector vaccine from Johnson and Johnson or the ChAdOx1-S recombinant vaccine from AstraZeneca, even if they had an mRNA vaccine as a booster). A chart review was conducted to assess the following parameters: age, sex, race, number of visits to the DFCM between 01/01/2021 and 05/15/2022, immunocompromising diagnoses, mRNA vaccination status, mRNA vaccination type, and number of mRNA vaccines received.

The initial EMR report identified 1067 patients with at least 1 qualifying diagnosis. Of these, patients were excluded for mislabeled diagnoses on their EMR (n = 26), having confidential and restricted patient records (n = 31), having no record of a visit to their

primary care physician during the study period (n = 94), or having received a non-mRNA COVID-19 vaccine (n = 29). The final sample used for analysis was 887 patients.

Analysis

Descriptive statistics were calculated. Paired *t* test were conducted to assess relationships between immunocompromised patients with 3 or more mRNA vaccine doses and those with 2 or less mRNA vaccine doses. PRISM was used to complete the study analyses (version 9.4.1).

Results

Sample characteristics can be found in Table 1. The majority of patients in the sample were Black (66.7%), above the age of 50 (82.1%), and male (55.9%). Solid tumor cancers were the most represented immunocompromising diagnoses in the sample (62.6%), followed by HIV/AIDS (23.8%), and patients on dialysis (10.6%).

Of the total n = 887 patients, n = 556 patients received 3 or more mRNA vaccines (62.7%). Eighty-three patients had no COVID-19 vaccines on record (9.4%; not included in Table 1). Overall,

Table 1. Demographic Information of Immunocompromised Patients (n = 887) by Vaccination Status

	Total		≥ 3 mRNA Vaccines		≤2 mRNA Vaccines		
	n	(%)	n	(%)	n	(%)	*p*-Value
Total	887	(100.0)	556	(62.7)	331	(37.3)	–
Race*							
White	227	(25.6)	170	(74.9)	57	(25.1)	0.1292
Black or African American	591	(66.7)	343	(58.0)	248	(42.0)	
Hispanic	43	(4.8)	28	(65.1)	15	(35.9)	
Asian	21	(2.4)	13	(61.9)	8	(38.1)	
American Indian or Alaskan Native	4	(0.5)	4	(100.0)	0	(0.0)	
Other/Unknown	7	(0.8)	3	(42.9)	4	(57.1)	
Age, y							
20–29	22	(2.5)	4	(18.2)	18	(81.9)	0.1124
30–39	48	(5.4)	14	(29.2)	34	(70.8)	
40–49	89	(10.0)	42	(47.2)	47	(52.8)	
50–59	184	(20.7)	112	(60.9)	72	(39.1)	
60–69	258	(29.1)	172	(66.7)	86	(33.3)	
70–79	203	(22.9)	145	(71.4)	58	(28.6)	
80+	83	(9.4)	67	(80.7)	16	(19.3)	
Sex							
Female	391	(44.1)	236	(60.4)	155	(39.6)	0.1738
Male	496	(55.9)	320	(64.5)	176	(35.5)	
Diagnosis†							
Hematologic cancers‡	12	(1.4)	9	(75.0)	3	(25.0)	0.2428
Solid tumor cancers§	555	(62.6)	371	(66.8)	184	(33.2)	
Autoimmune disorders‖	30	(3.4)	19	(63.3)	11	(36.7)	
Solid organ transplant recipients¶	46	(5.2)	29	(63.0)	17	(37.0)	
HIV/AIDS	211	(23.8)	122	(57.8)	89	(42.2)	
Patients on Dialysis	94	(10.6)	43	(45.7)	51	(54.3)	

Notes. *Some patients identified with more than one race, so the values in this category add up to greater than the total sample size.
†Patients may have had more than one diagnosis, so the values in this category add up to greater than the total sample size.
‡Diagnoses included in this category: diffuse large B-cell lymphoma, follicular lymphoma, multiple myeloma, chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML).
§Diagnoses included in this category: breast cancer, lung cancer, prostate cancer, colorectal cancer, melanoma, bladder cancer, head and neck cancer.
‖Diagnoses included in this category: autoimmune hepatitis, psoriatic arthritis, spondyloarthritis, ankylosing spondylitis, rheumatoid arthritis, primary biliary cholangitis, dermatomyositis, systemic lupus erythematosus, primary Sjögren's syndrome, systemic sclerosis.
¶Transplants included in this category: kidney, liver, heart/lung, pancreas.

those who received 3 or more COVID-19 mRNA vaccines were predominately Black or African American (61.7%), between the ages of 60 and 69 (30.9%), and male (57.6%). However, when accounting for the sample size of each demographic factor, proportionally more white patients received 3 or more vaccines than Black or African American patients (74.9% vs 58.0%), patients equal to or older than the age of 80 had the largest proportion of patients with 3 or more COVID-19 vaccines (80.7%), and more females than males received 3 or more mRNA vaccines (81.1% vs 64.5%). Of the 331 patients with 2 or less mRNA vaccine doses, almost 75% of them were Black, 70.1% were equal to or older than the age of 50, and 53.2% were male. Accounting for the sample size of each group, proportionally more Black or African Americans received 2 or less mRNA vaccines than White patients (42.0% vs 25.1%). Paired *t* test analyses were not significant when comparing vaccination status by race, age, sex, or immunocompromising diagnosis.

Discussion

The purpose of our study was to assess COVID-19 mRNA vaccination patterns among immunocompromised patients at a large, urban primary care setting. A large portion of the sample only received 2 or less mRNA vaccine doses, with variations present in the number of vaccine doses received among different races, age groups, and sexes, suggesting that there is work to be done to improve vaccination rates in this vulnerable population.

To contextualize these findings, it is important to discuss how this clinic addressed COVID-19 vaccination when vaccines became available to the public. The Jefferson DFCM was not authorized to provide COVID-19 vaccines during the full length of the study period. Initially, patients were referred to a special COVID-19 vaccination site run by the city's Department of Public Health (DPH). However, in June 2021, the city's DPH operated a COVID-19 vaccination program in our office space but provided vaccination only on Saturdays and late evenings, after the regular clinic hours were completed. Patients interested in receiving COVID-19 vaccines at our clinic therefore had to make a separate visit to receive this service. Many of our patients may also have had more contact with specialty clinics than with their primary care provider at our site given their immunocompromising diagnoses. None of the local oncology offices or other specialty offices (including even Infectious Diseases) provided COVID-19 vaccines during the study period, but many (or all) likely recommended that these patients receive them at the city-run COVID-19 vaccine clinics. The fact that physicians had to refer patients elsewhere for COVID-19 vaccinations during this study period likely contributed to less-than-optimal vaccination rates in this study.

Throughout the course of the COVID-19 pandemic, Black and African American communities have been disproportionately impacted by COVID-19 infection and death.[16,17] COVID-19 vaccination rates are also lower among Black patients in the United States than other races.[18] Our data followed a similar trend, with more than 40% of the Black or African American group in our sample receiving 2 or less vaccines. This disparity in vaccination among Black patients is likely due to several interplaying factors, such as access to vaccination, a sense of personal invulnerability to COVID-19 infection, or hesitancy stemming from institutional mistrust founded in historic and personal experiences of racism, to name a few.[17,19–21] Given the additional factor of immunocompromised status in our population, it is especially important for primary care physicians to actively discuss vaccination with their Black or African American patients through education and motivational interviewing, with the goal of combatting misinformation while acknowledging and addressing the historic mistrust of vaccines and of the health care system.[22]

This study has several strengths. By assessing the COVID-19 vaccination trends of immunocompromised patients in a large, urban, primary care setting, we were able to provide primary care physicians with a broad view of vulnerable patient populations that can be targeted for vaccination education and reminders. This study also assessed many immunocompromising conditions commonly seen in the primary care setting using lists of immunocompromising diagnoses previously published in the field of COVID-19 literature.[14,15] However, limitations persist. When categorizing patients into diagnosis groups, we were unable to stratify the sample based on degree of immune dysfunction. Because the magnitude of immunocompromise associated with a given diagnosis can vary greatly, some patients require more protection in the form of vaccination than other patients in the same diagnosis category, which could bias vaccine

practices among patients. Our study also assessed patients who received only mRNA COVID-19 vaccine doses, excluding the patients who received other non-mRNA COVID-19 vaccines, such as the JNJ-78436735 viral vector vaccine, even if they were boosted with an mRNA vaccine. This decision was made to align with the Food and Drug Administration (FDA), which strongly encourages mRNA primary series and booster doses in immunocompromised patients.[13] These exclusions were also made due to the presence of confusion among providers and patients over recommended sequencing and timing of mixing COVID-19 vaccine during the study period. However, by excluding immunocompromised patients who received non-mRNA vaccines like the Johnson & Johnson vaccine, there is a chance we could have removed patients who were, for example, vaccine hesitant and were only comfortable receiving 1 dose of a vaccine, thus potentially impacting our sample. Lastly, the CDC changed the vaccination requirements for immunocompromised patients from 2 doses to 3 doses of an mRNA vaccine in the middle of the study period (August 2021). Therefore, some patients who were last seen by their DFCM primary care provider in late-2021 could have been fully vaccinated by CDC standards. Others who received their second dose in early 2022 may not have been due for their third dose until after the study period. This could have placed some patients in the 2 or less mRNA vaccine group even though they were up to date with their vaccinations for immunocompromised patients at the time of their last visit.

Although the majority of immunocompromised patients in our study received 3 or more doses of a COVID-19 mRNA vaccine, disparities in vaccination rates exist, especially when comparing White and Black patients. The fact that primary care physicians at our clinic had to refer patients elsewhere for COVID-19 vaccines during this period likely contributed to the less-than-optimal vaccination rates for the duration of our study. Primary care physicians are the most important influence on patients' uptake of vaccines. COVID-19 vaccine rates would likely have been higher if COVID-19 vaccines were made available in the primary care office at the time of the patient's visit with their trusted physician. We hope that this study joins other existing studies about racial disparities in COVID-19 vaccination rates in helping primary care physicians shape the way in which they target their COVID-19 vaccination and education, especially when it comes to immunocompromised populations. Future studies could include COVID-19 vaccination and infection trends within each immunocompromising diagnosis category, for example, by stratifying by degree of immune dysfunction to determine if that factor impacts COVID-19 vaccination practices and infection rates among immunocompromised populations.

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