Characteristics of Postvaccination Coronavirus Disease 2019 Hospitalizations Prior to Booster Vaccines

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This analysis describes clinical characteristics and outcomes of 128 fully vaccinated patients hospitalized with coronavirus disease 2019 (COVID-19) prior to booster vaccines. We found that 27% were asymptomatic, 52% required intensive care, and 15% died from COVID-19. Most (89.2%) fully vaccinated patients hospitalized with symptomatic COVID-19 were ≥65 years old and/or severely immunosuppressed.

Keywords. COVID-19; hospitalization; SARS-CoV-2; vaccination.

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) plays an important role in reducing severe disease caused by coronavirus disease 2019 (COVID-19). Data from Los Angeles County from May to July 2021 found that unvaccinated persons were 29.2 times more likely to be hospitalized for COVID-19 compared to fully vaccinated persons [1]. The overall age-adjusted vaccine effectiveness (VE) against hospitalization during that same period in New York State was found to be 91.9%–95.3% [2]. Despite this high protection conferred from vaccination, postvaccination hospitalizations do occur, although limited descriptive data exist [3, 4]. Importantly, these studies included time periods prior to the widespread emergence of the Delta variant. We aimed to evaluate clinical characteristics and outcomes of fully vaccinated patients hospitalized with COVID-19 after the emergence of the Delta variant, prior to the Omicron variant, and prior to use of booster vaccines.

METHODS

We conducted a retrospective review of all patients admitted with COVID-19 to 8 diverse western Pennsylvania hospitals (including both tertiary care and community-based hospitals) within the Allegheny Health Network (AHN) between 15 July and 31 August 2021. Exempt status was granted by the AHN Institutional Review Board. Patients were identified using the electronic health record by extracting all patients with a positive SARS-CoV-2 test during the study time period, or if they had an active COVID-19 designation by the AHN infection prevention department for patients diagnosed outside the health system. Patients were included if they had COVID-19 during their hospitalization. Patients aged <18 years were excluded. Patients are not routinely tested for SARS-CoV-2 on admission at AHN, but only tested per the discretion of the treating provider, if a long-term care facility protocol requires testing prior to placement, or when a department protocol requires testing prior to a procedure. For patients with multiple hospitalizations, each admission was reviewed. Demographic information, vaccination data, comorbidities, and clinical data were manually collected via review of the electronic health record, utilizing a standardized data collection instrument.

The primary aim was to describe the characteristics of fully vaccinated persons admitted with COVID-19. Secondary aims included determining estimated SARS-CoV-2 VE against hospitalization with COVID-19, need for intensive care unit (ICU)-level care, need for mechanical ventilation, and in-hospital mortality. VE was estimated using the formula

\[ \text{VE} = 1 - \frac{\text{odds of vaccination among cases}}{\text{odds of vaccination among population}} \]

where the denominator is adjusted for age, sex, race, pre-existing conditions, and hospital type.

SARS-CoV-2 vaccination status was recorded, including the specific vaccine type (mRNA-1273 [Moderna], BNT162b2 [Pfizer-BioNTech], or Ad.26.COV2.S [Janssen]) with vaccination dates. Patients were considered fully vaccinated if symptom onset or positive SARS-CoV-2 testing was at least 14 days after their final dose. Severe immunosuppression was defined as use of chronic immunosuppressive therapy (if corticosteroids, equivalent of >20 mg prednisone daily), human immunodeficiency virus with CD4 cell count <350 cells/µL, active malignancy with receipt of chemotherapy within the past year, or prior solid organ transplant or hematopoietic stem cell transplantation.

RESULTS

During the analysis period, 473 patients were hospitalized with COVID-19. Of these, 128 were fully vaccinated against...
SARS-CoV-2. The other 345 were either unvaccinated or did not complete full vaccination at least 14 days prior to their final vaccine dose. Of the 128 fully vaccinated patients, 84 were vaccinated with BNT162b2, 29 were vaccinated with mRNA-1273, and 15 were vaccinated with Ad26.COV2.S. There was an average of 4.5 months (range, 1–7 months) after vaccination prior to hospitalization. All but 4 completed their vaccination within the 6 months preceding hospitalization (all received BNT162b2). No patients had received a booster dose. Of the 128 fully vaccinated patients, 93 (72.7%) were symptomatic from COVID-19 (Table 1). Of the 35 patients who were asymptomatic for the duration of their hospitalization, 25 (71.4%) were tested due to placement in a long-term care facility per protocols at most local skilled nursing facilities.

The 93 symptomatic postvaccination patients had a mean age of 73.2 years (range, 37–94 years) with 77 (82.8%) ≥65 years of age (Table 1). The mean body mass index (BMI) was 31.7 kg/m² (range, 18.4–55.6 kg/m²) with the majority of patients (52.7%) having a BMI of >30 kg/m². Twenty-three (24.7%) were severely immunosuppressed. Of the other 70 patients, 60 were ≥65 years

| Characteristic | All Hospitalized Patients (n = 128) | Symptomatic Patients (n = 93) |
|---------------|----------------------------------|-----------------------------|
| Demographics  |                                  |                             |
| Age, y, mean (range) | 72.8 (19–94) | 73.2 (37–94) |
| ≤39           | 3 (2.3)                           | 1 (1.1)                     |
| 40–54         | 8 (6.3)                           | 7 (7.5)                     |
| 55–64         | 13 (10.2)                          | 8 (8.6)                     |
| 65–74         | 40 (31.3)                          | 30 (32.3)                   |
| ≥75           | 64 (50)                            | 47 (50.5)                   |
| Female sex    | 67 (52.3)                          | 47 (50.5)                   |
| Comorbidities |                                  |                             |
| Body mass index, kg/m² |                     |                             |
| <30           | 69 (53.9)                          | 44 (47.3)                   |
| 30–34.9       | 26 (20.3)                          | 22 (23.7)                   |
| 35–39.9       | 16 (12.5)                          | 14 (15.1)                   |
| ≥40           | 17 (13.3)                          | 13 (14)                     |
| Severe immunosuppression | 30 (23.4)     | 23 (24.7)                   |
| Solid organ transplant recipient | 10           | 7                           |
| Hematologic malignancy with receipt of chemotherapy in past year | 7            | 7                           |
| Autoimmune disease on immunosuppressive therapy | 7           | 6                           |
| Active cancer with receipt of chemotherapy in past year | 4            | 2                           |
| Other diagnosis on immunosuppressive therapy | 2           | 1                           |
| Hypertension  | 95 (74.2)                          | 71 (76.3)                   |
| Hyperlipidemia | 62 (48.4)                          | 42 (45.2)                   |
| Chronic lung disease | 51 (39.8)     | 43 (46.2)                   |
| Diabetes mellitus | 46 (35.9)                  | 37 (39.8)                   |
| Chronic kidney disease | 30 (23.4)     | 24 (25.8)                   |
| Coronary artery disease | 30 (23.4)     | 23 (24.7)                   |
| Congestive heart failure | 30 (23.4)     | 23 (24.7)                   |
| Atrial fibrillation | 26 (20.3)                     | 18 (19.4)                   |
| Cancer without receipt of chemotherapy in past year | 21 (16.4)     | 15 (16.1)                   |
| Cerebral vascular accident/transient ischemic attack | 14 (10.9)     | 9 (9.7)                     |
| Autoimmune disease without active immunosuppressive therapy | 10 (7.8)      | 6 (6.5)                     |
| Peripheral vascular disease | 9 (7.0)         | 6 (6.5)                     |
| Chronic liver disease | 8 (6.3)              | 6 (6.5)                     |
| Dementia       | 7 (5.5)                            | 4 (4.3)                     |
| Seizure        | 7 (5.5)                            | 3 (3.2)                     |
| Hematologic malignancy without receipt of chemotherapy in past year | 3 (2.3)        | 3 (3.2)                     |
| Clinical course|                                  |                             |
| Presence of pulmonary symptoms | 79 (61.7)     | 79 (84.9)                   |
| Receipt of >4 L/minute of supplemental oxygen during hospitalization | 41 (32.0)     | 41 (44.1)                   |
| Required ICU-level care | 66 (51.6)         | 66 (71.0)                   |
| Required mechanical ventilation during hospitalization for COVID-19 | 14 (10.9)     | 14 (15.1)                   |
| In-hospital death due to COVID-19 | 19 (14.8)         | 19 (20.4)                   |

Data are presented as No. (%) unless otherwise indicated.
Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit.
old with numerous comorbidities. Only 10 (10.8%) fully vaccinated patients with symptomatic COVID-19 were <65 years old and without severe immunosuppression. All patients had at least 1 comorbidity. The majority of patients (76.3%) had hypertension. Other comorbidities can be found in Table 1.

Of the 93 symptomatic patients, 79 (84.9%) had pulmonary symptoms with 41 (44.1%) requiring >4 L/minute of supplemental oxygen at any point during their hospitalization. Fourteen (15.1%) patients were placed on mechanical ventilation and 19 (20.4%) died during hospitalization due to COVID-19. Of the 19 patients with in-hospital death due to COVID-19, 5 were severely immunosuppressed. Of the other 14 patients, 11 were ≥65 years of age and all had numerous comorbidities. Included in the 3 patients <65 years of age without severe immunosuppression was a 52-year-old patient with Down syndrome and advanced dementia vaccinated with BNT162b2 6 months prior; a 53-year-old patient with diabetes mellitus, hypertension, chronic kidney disease, and chronic liver disease vaccinated with BNT162b2 4 months prior; and a 64-year-old patient with diabetes mellitus, hypertension, hyperlipidemia, and coronary artery disease vaccinated with Ad.26.COV2.S 3 months prior. Details on all in-hospital deaths can be found in Supplementary Table 1.

VE against hospitalization, need for ICU care, mechanical ventilation, and in-hospital mortality for the entire cohort was estimated to be 84.5%, 85.1%, 86.6%, and 83.1%, respectively. Vaccination was found to be >91% protective against hospitalization for all age groups under 70. VE breakdowns by age are shown in Table 2. No fully vaccinated patient under the age of 50 needed mechanical ventilation or died from COVID-19.

**DISCUSSION**

Our report adds to the limited published data describing the clinical characteristics of fully vaccinated patients hospitalized with COVID-19 prior to booster vaccines. Juthani et al recently described 54 fully vaccinated patients hospitalized from 23 March to 1 July 2021 in Connecticut [3], while Brosh-Nissimov et al described 152 fully vaccinated patients hospitalized 18 January to 20 April 2021 in Israel [4]. A common finding among the 3 cohorts is that at least 1 in 5 patients were either asymptomatic or admitted for a non–COVID-19 reason. Juthani et al found that 46% of patients were asymptomatic, while Brosh-Nissimov et al found that 19% of patients were admitted for a medical problem unrelated to COVID-19. We found 27% of patients to be asymptomatic and detected while screening for other reasons such as placement into long-term care or preprocedure testing. Of note, our health system does not test all patients on admission for SARS-CoV-2. With regard to severe/critical illness and mortality, Juthani et al found that 26% of patients had severe/critical illness and a 5.5% mortality rate, whereas Brosh-Nissimov et al found 61% of patients to have severe/critical illness and a mortality rate of 22%. We found that 52% of patients in our cohort required ICU-level care, and 15% died in the hospital. All 3 cohorts found the majority of patients to be elderly. Juthani et al reported the average age of patients with severe or critical illness to be 80.5 years, Brosh-Nissimov et al reported the median age to be 71.1 years, and our cohort average age was 72.8 years. Brosh-Nissimov et al reported 40% to be immunosuppressed, whereas we found 23.4% of our cohort to be severely immunosuppressed. Importantly, our study was performed entirely during a time period where the Delta variant constituted nearly all cases in the United States [6]. Also, no patients in our study had received a booster dose as they had yet to be widely authorized.

Our report also contributes to the large amount of data showing substantial protection from vaccination against hospitalization and death from COVID-19. According to the Centers for Disease Control and Prevention, fully vaccinated persons have consistently been hospitalized at a rate of <5 per 100 000 persons, compared to unvaccinated persons hospitalized at a rate of >50 per 100 000 persons during our study time period [7]. We found that VE was lower among those aged ≥70 years for protection against hospitalization, and those ≥80 years for the need of ICU-level care, relative to younger age groups. No fully vaccinated patient under the age of 50 required mechanical ventilation or died from COVID-19.

Our study has several important limitations. While data were collected among 8 different hospitals in AHN, they are all geographically located in western Pennsylvania, and findings may

| Age Group, y | VE Against Hospitalization | VE Against ICU Care | VE Against Mechanical Ventilation | VE Against In-Hospital Mortality |
|--------------|---------------------------|--------------------|-----------------------------------|-------------------------------|
| ≥80          | 72.5%                     | 67.8%              | 86.6%                             | 86.6%                         |
| 70–79        | 86.7%                     | 90.5%              | 83.7%                             | 90.2%                         |
| 60–69        | 91.5%                     | 92.5%              | 96.2%                             | 92.5%                         |
| 50–59        | 96.1%                     | 95.2%              | 89.5%                             | 83.0%                         |
| 40–49        | 95.3%                     | 96.8%              | 100.0%                            | 100.0%                        |
| 30–39        | 98.2%                     | 100.0%             | None available                    | None available                |
| ≤29          | 92.7%                     | 88.5%              | None available                    | None available                |
| All patients | 84.5%                     | 85.1%              | 86.6%                             | 83.1%                         |

Abbreviations: ICU, intensive care unit; VE, vaccine effectiveness.
not be generalizable to other regions. Our health system does not test all patients for COVID-19 routinely on admission, but it is standard practice that patients are tested prior to placement in long-term care. This is the reason for diagnosis in most of our asymptomatic cases, which may influence the characteristics of our total cohort relative to institutions with broader testing strategies. Because data for non–fully vaccinated patients with symptomatic COVID-19 were not available for this analysis, we were unable to calculate VE against symptomatic hospitalization. Our VE calculations were also unable to account for immunity from prior infection or partial vaccination in the group of non–fully vaccinated patients, which may underestimate VE.

CONCLUSIONS

We reviewed 128 fully vaccinated patients hospitalized with COVID-19 prior to booster vaccines and found that 27% were asymptomatic, 52% required ICU care, and 15% died due to COVID-19. Most (89.2%) fully vaccinated patients with symptomatic COVID-19 were ≥65 years old and/or severely immunosuppressed. No fully vaccinated patient under the age of 50 years required mechanical ventilation or died from COVID-19.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Patient consent statement. This study did not include factors necessitating patient consent. Exempt status was granted by the AHN Institutional Review Board.

Potential conflicts of interest. All authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Griffin JB, Haddix M, Danza P, et al. SARS-CoV-2 infections and hospitalizations among persons aged ≥16 years, by vaccination status—Los Angeles County, California, May 1–July 25, 2021. MMWR Morb Mortal Wkly Rep 2021; 70:1170–6.
2. Rosenberg ES, Holtgrave DR, Dorabawila V, et al. New COVID-19 cases and hospitalizations among adults, by vaccination status—New York, May 3–July 25, 2021. MMWR Morb Mortal Wkly Rep 2021; 70:1306–11.
3. Juthani PV, Gupta A, Borges KA, et al. Hospitalisation among vaccine breakthrough COVID-19 infections. Lancet Infect Dis 2021; 21:1485–6.
4. Brosh-Nissimov T, Orenbuch-Harroch E, Chowers M, et al. BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully vaccinated hospitalized COVID-19 patients in Israel. Clin Microbiol Infect 2021; 27:1652–7.
5. Pennsylvania Department of Health. COVID-19 vaccine dashboard. https://www.health.pa.gov/topics/disease/coronavirus/Vaccine/Pages/Dashboard.aspx. Accessed 31 August 2021.
6. Centers for Disease Control and Prevention. Variant proportions. https://covid.cdc.gov/covid-data-tracker/#variant-proportions. Accessed 15 September 2021.
7. Centers for Disease Control and Prevention. Age-adjusted rates of COVID-19-associated hospitalizations by vaccine status in adults aged ≥18 years, January–September 2021. https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination. Accessed 26 November 2021.