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RESEARCH LETTER

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Delirium after COVID-19 vaccination in nursing home residents: A case series

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INTRODUCTION

Older adults in nursing homes (NH) are particularly vulnerable to severe illness and death due to COVID-19 infection. Vaccination is associated with reduced risk of infection,[1] and vaccinated individuals who develop COVID-19 infection are less likely to experience severe symptoms or death.[2] The rate of adverse events after vaccination has been minimal to none.[3] However, there have been reports of delirium in older adults after COVID-19 vaccination.[4,5] The objective of this case series was to describe the frequency of delirium and its severity among NH residents after COVID-19 vaccination.

METHODS

Design, setting, participants

This study was conducted at a 514-bed NH in 2021 during 1–2 day initiatives to provide COVID-19 vaccinations to residents. It was ancillary to a larger study, the Better Assessment of Illness (BASIL) II study, designed to improve the assessment of delirium in older adults. Institutional Review Board approval was obtained at the NH and affiliated medical center.

Participants were NH residents who were ≥70 years old, English-speaking, and expected to stay in the NH for at least 3 months. Residents who were non-verbal, blind/deaf, non-English-speaking, had active alcohol abuse, or were COVID-19+, were excluded. Participants or their legal surrogates provided informed consent.

Assessment

After enrollment participants were followed for conditions that could precipitate a change in health status. For the current study, COVID-19 vaccination was considered a precipitating condition, and 1 day after vaccination participants were screened for the presence of items in the Confusion Assessment Method-Severity (CAM-S)[6] (see Table 1). Those who endorsed any of these items and a random sample of those who endorsed none were selected for structured assessment.

Structured assessments were conducted in-person and included the Severe Illness Battery-8 (SIB-8),[7] the

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Montreal Cognitive Assessment (MoCA),[8] the Confusion Assessment Method (CAM),[9] and CAM-S severity score.[6] Presence of delirium was determined using the Diagnostic and Statistical Manual of Mental Disorders (5th edition; DSM-5),[10] based on testing at baseline and post-vaccination. Subsyndromal delirium was defined as new onset of delirium symptoms without fulfilling DSM-5 criteria. If delirium symptoms were present after vaccination, a repeat assessment was conducted 2 weeks later.

Demographic information, prior history of delirium, and baseline major neurocognitive disorder (dementia) or minor neurocognitive disorder (mild cognitive impairment) using DSM-5 criteria were recorded.

TABLE 1 CAM-S symptoms 1 day after COVID-19 vaccination in 4 cases with delirium

Case	1	2	3	4
Acute onset and fluctuating course	1	1	1	1
Inattention	0	1	1	2
Disorganized thinking	0	0	0	0
Altered level of consciousness	1	1	1	1
Disorientation	0	2	1	1
Memory impairment	2	2	2	2
Perceptual disturbances	1	0	0	1
Psychomotor agitation	0	0	0	0
Psychomotor retardation	0	0	2	1
Altered sleep–wake cycle	1	1	2	1

Note: 0 = no; 1 = yes, mild; 2 = yes, marked.

Statistical analyses

Descriptive statistics were used to characterize baseline characteristics and post-vaccination delirium outcomes. Paired *t* tests were used to test the change in cognitive function scores across time points. Fisher's exact tests were conducted to test whether post-vaccination delirium was associated with having dementia at baseline or a prior history of delirium.

RESULTS

Forty participants were included; for 39 participants it was the third vaccination; for 1, the second vaccination. The average age was 82 ± 7 (SD) years; 55% were female, 43% were non-White, and 13% indicated Latino/Hispanic

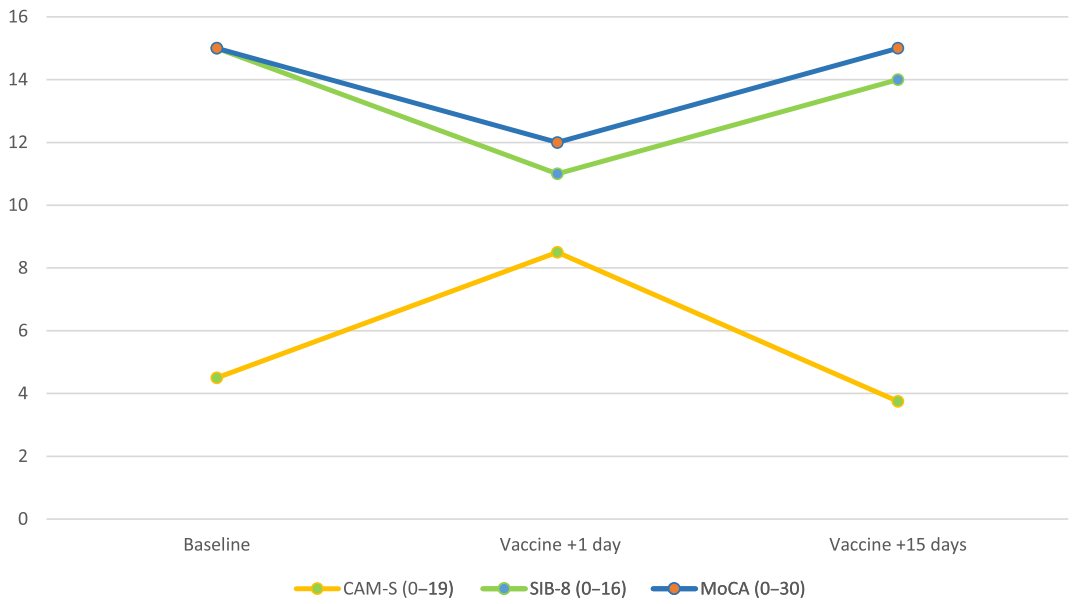

FIGURE 1 Average CAM-S, SIB-8, and MoCA scores of NH residents who experienced delirium 1 day after receiving a COVID-19 vaccine (n = 4). CAM-S = Confusion Assessment Method-Severity; 10-item measure of delirium severity; range: 0–19, higher scores = greater delirium severity. At minimum, people who are delirious have a score of 3 (items endorsed: acute change or fluctuation and inattention, and either disorganized thinking or altered level of consciousness). Any additional points may indicate the worsening of delirium severity.[6] SIB-8 = Severe Impairment Battery; 8-item cognitive measure for people with moderate to severe dementia; range: 0–16, higher scores = better cognition. A decline of >1 point within a year may indicate a clinically meaningful change in cognition.[7] MoCA = Montreal Cognitive Assessment; 30-item cognitive measure for people with mild cognitive impairment or mild to moderate dementia; range = 0–30, higher scores = better cognition. The clinical cut-off score is 26, 18–25: mild cognitive impairment, ≤17: dementia. A decline of >1.7 over 3.5 years may indicate clinically significant change in cognition.[11]

ethnicity. At baseline 65% had major neurocognitive disorder, and 35% had minor neurocognitive disorder. Seven (18%) had a prior history of delirium.

The day following COVID-19 vaccination, three (7.5%) had delirium and 1 (2.5%) had subsyndromal delirium (Table 1), for a total of 10% (95% confidence interval 3%–24%). The day following vaccination, these four cases had elevated mean CAM-S scores (8.8 ± 1.5 vs 4.5 ± 1.9; $p = 0.003$) and reduced MOCA scores (12 ± 4.1 vs 15 ± 4.2; $p = 0.014$) relative to baseline. None had competing causes of delirium, and all delirium resolved and cognitive scores returned to baseline at 2 weeks (Figure 1). The SIB-8 scores followed the same pattern.

In stratified analyses, 3 of 26 (12%) with versus 1 of 14 (7%) without dementia experienced delirium ($p = 0.56$), and 0 of 7 (0%) with and 4 of 33 (12%) without a prior history of delirium experienced delirium ($p = 0.45$).

DISCUSSION

In a general population, delirium is uncommon after COVID-19 vaccination,[3] but cases of older adults with delirium after COVID-19 vaccination have been reported.[4,5] Vaccination may cause systemic inflammation that adversely affects brain function.

In the current study, delirium or subsyndromal delirium of mild to moderate severity was identified in 10% of NH residents the day after vaccination, with no potential competing explanation. Strengths of this study are the inclusion of older adults with physical and cognitive impairment, underrepresented minorities, baseline assessments to facilitate determination of a change in cognition, and rigorous cognitive testing.

In this study, delirium after COVID-19 vaccination resolved without complications, which contrasts with complications of COVID-19 infection itself. Thus, the risk–benefit ratio strongly supports vaccination in this population. Nevertheless, because of the heightened risk of delirium and its potential complications in NH residents, clinicians and staff should monitor for delirium after COVID-19 vaccination.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

All authors meet the criteria for authorship stated in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: study concept and design: Kenneth Boockvar, Wingyun Mak, Sharon Inouye; acquisition of data: Wingyun Mak, Abena Prempeh, Kenneth S. Boockvar; analysis and interpretation of data: all authors; drafting of the manuscript: Wingyun Mak; critical revision of the manuscript for important intellectual content and final approval: all authors.

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The sponsors had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

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