JAMDA 25 (2024) 105251

JAMDA

journal homepage: www.jamda.com

Original Study

Delirium Incidence and Predictors in SARS-CoV-2 Vaccinated Residents in Long-Term Care Facilities (LTCF): Insights from the GeroCovid Vax Study

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Keywords:
COVID-19
vaccine
older adults
long-term facilities
frailty

A B S T R A C T

Objective: SARS-CoV-2 vaccination can bring an important benefit for older people in terms of reduction of mortality and hospitalization; however, reports of rare adverse effects like altered consciousness and delirium among this demographic have raised concerns. This study aimed to assess delirium incidence post-SARS-CoV-2 vaccination and its predictors in older residents across 60 Italian long-term care facilities (LTCFs).

Design: This is a prospective cohort study considering data from GeroCovid Vax, a multicenter cohort study jointly performed by the Italian Society of Gerontology and Geriatrics (SIGG) (Florence, Italy) and the Italian National Institute of Health (Istituto Superiore di Sanità—ISS, Rome, Italy), and sponsored by the Italian Medicines Agency (Agenzia Italiana del Farmaco—AIFA).

Setting and Participants: GeroCovid Vax enrolled LTCFs residents aged ≥60 who received at least 1 anti −SARS-CoV-2 vaccine dose.

Methods: Baseline data covered sociodemographic details, chronic diseases, medications, nutritional status, cognitive and functional assessments, mobility, and frailty. Delirium was assessed post-first, second, and booster vaccine doses using DSM-5 criteria. Data analysis involved descriptive statistics, multivariate logistic regression, and network analysis.

C.O. and M.B.Z. share first authorship of this paper.

All authors confirm that they had full access to all the data in the study and accept responsibility to submit for publication.

No funding was received for conducting this study.

Ethical approval was not required for this secondary research.

All patients have provided consent for the use of their data in anonymized form for the purposes of the study.

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https://doi.org/10.1016/j.jamda.2024.105251

Results: A total of 2521 participants (mean age 83.10 ± 9.21 years, 70.7% female) were analyzed. Delirium incidence post-first, second, and booster doses was 3.5%, 1.6%, and 1.5%, respectively. Age, preexisting cognitive disorders, and frailty were significant predictors of delirium, with odds ratios (ORs) of 1.70 (95% CI, 1.08−2.77), 2.05 (95% CI, 1.40−2.97), and 1.77 (95% CI, 1.25−2.52), respectively. Prior use of antipsychotics (OR, 1.75; 95% CI, 1.22−2.51) and antidepressants (OR, 1.77; 95% CI, 1.25−2.52) correlated significantly with delirium. Network analysis indicated a strong association between anorexia and delirium.
Conclusion and Implications: Post-vaccination delirium is infrequent and decreases with subsequent doses. Timely assessments for frailty and cognitive impairment could aid in stratifying delirium risk among LTCF residents, facilitating enhanced prevention measures and close monitoring for delirium indicators.

Throughout the COVID-19 pandemic, the older population has consistently exhibited the highest morbidity and mortality rates,[1] with a notable impact on residents of long-term care facilities (LTCFs) in Europe. Within these facilities, more than 800,000 COVID-19 deaths have been recorded, with more than 88% occurring in individuals aged 65 and older.[2]

Various factors, including high occupancy density, communal living arrangements, resource inadequacies, frailty status, and outdated infrastructure, have heightened the vulnerability of LTCF residents to COVID-19.[2,3] In response to the outbreaks, various measures have been proposed, including social interventions (such as lockdowns, quarantine, and social isolation), and vaccination campaigns.[4] Globally, vaccines targeting SARS-CoV-2, using mRNA, viral vectors, and inactivated viruses, have played a pivotal role in combating the spread of the virus.[4] Despite the proven efficacy of vaccines, during the COVID-19 pandemic, vaccine hesitancy, particularly prevalent among older individuals,[4,5] remains a significant obstacle to achieving herd immunity.[6] A recent study identified older age as a factor associated with vaccination skepticism, aligning with findings from a systematic review emphasizing concerns about vaccine safety as a primary driver of hesitancy.[7] Notably, phase III studies on SARS-CoV-2 vaccines included only a minority of participants older than 75 years, potentially overlooking atypical adverse reactions in this cohort. Isolated reports have documented rare cases of altered consciousness, encephalopathy-like symptoms, delirium, and memory disturbances following vaccination.[8]

Delirium is a syndrome marked by a sudden mental change, attention deficits, and altered arousal. It arises swiftly, demonstrates fluctuations, and is typically associated with an underlying cause.[9,10] Although delirium can affect individuals across various age groups and health statuses, there is an elevated risk for those with advanced age, functional limitations, substantial comorbidities, and dementia.[9] In such scenarios, even mild stressors such as vaccination can serve as triggers for delirium. Although other studies have detailed instances of delirium in both outpatients and nursing home residents,[11,12] a study involving 17,449 older individuals with dementia who received at least 1 vaccine dose reported no apparent increase in delirium risk.[13] However, comprehensive investigations involving large older populations are lacking, hindering definitive conclusions regarding the connection between vaccination and delirium.

Given these premises, this study aimed to (1) assess the incidence of delirium within 1 week following SARS-CoV-2 vaccinations (first, second, and booster doses), (2) determine predictors of post-vaccination delirium in LTCF residents, and (3) elucidate connections between recorded post-vaccination symptoms and delirium within the study cohort.

Materials and Methods

Study Population

This is a prospective cohort study that used data from GeroCovid Vax, a multicenter cohort study jointly performed by the Italian Society of Gerontology and Geriatrics (SIGG) (Florence, Italy) and the Italian National Institute of Health (Istituto Superiore di Sanità—ISS, Rome, Italy), and sponsored by the Italian Medicines Agency (Agenzia Italiana del Farmaco—AIFA). GeroCovid Vax is focused on evaluating the efficacy and safety of SARS-CoV-2 vaccination in older residents of Italian LTCFs. This study enrolled older LTCF residents (aged ≥60 years) undergoing vaccination (at least 1 dose of the anti−SARS-CoV-2 vaccine) and with an estimated life expectancy and expected stay in the LTCF of ≥3 months. All participants were followed prospectively based on their vaccination status and subsequent outcomes. The study protocol details have been previously published.[14]

Ethics Committee

The study obtained approval from the Ethical Committee at the Spallanzani Institute (permission no. 264/2021; 26 January 2021; Rome, Italy) and local ethics committees at the respective participating sites.

Data Collection

The data collection for GeroCovid Vax started in January 2021, overseen by physicians and researchers specialized in the geriatric field, at the participating sites. These professionals underwent training for the accurate collection and recording of data using an e-registry developed by Bluecompanion Ltd (London, UK).

Baseline data for each individual were gathered 7 days before the administration of the initial vaccine dose, with subsequent follow-up data collected at specific intervals (7 days after the first dose, the second dose, and the booster dose). For all participants, the following information was collected: sociodemographic characteristics (age, sex, and ethnicity), lifestyle details, chronic diseases, prescribed medications, nutritional status, functional and cognitive assessments, mobility function, and frailty status.[14,15] Mobility function was categorized based on walking ability (mostly bedridden but occasionally sits in a wheelchair and/or completely bedridden; moves around in a wheelchair and/or is accompanied; walks independently or with a cane and/or walker). Frailty status was evaluated according to Pedone et al,[16] considering the presence of at least 2 of the following anamnestic criteria: unintentional weight loss (>4.5 kg in the past year), exhaustion (ie, feeling the need for effort in daily tasks for >3 days in the previous week), and reduced physical activity (engaging in <2 to 4 hours of light exercise weekly). Both frailty status and mobility level were further summarized into categorical variables denoting the presence or absence of frailty and the level of mobility (0: Completely dependent on others for mobility, lying in bed most of the time; 1: Mobility possible only with a wheelchair; 2: Can walk independently or with a walking aid - cane or walker).

COVID-19—Vaccination Procedures and Adverse Events Reporting

The COVID-19 vaccination campaign in Italian LTCFs began at the end of December 2020, primarily using mRNA vaccines, namely Moderna mRNA-1273 or Cominarty BNT162b2. National guidelines recommended a single vaccine dose for residents with a previous SARS-CoV-2 infection within the past 6 months; otherwise, a 2-dose vaccination cycle was prescribed. The third dose, functioning as a booster, was specifically recommended for older individuals (older than 60), those with chronic pathologies, health care workers, and the armed forces.[17] Detailed records of the date, type, and number of administered SARS-CoV-2 vaccine doses were compiled for each participant. Following each dose, trained research personnel assessed, based on a standardized procedure, the presence of various signs and symptoms, including fever, low-grade fever, or chills; muscle weakness and muscle/joint pain; difficulty in breathing, cough, sneezing, increased heart rate or blood pressure; anorexia, nausea, vomiting, or diarrhea; general dizziness or weakness; headache, confusion, delirium, insomnia, or significant peripheral nervous system reactions (such as transverse myelitis or Guillain Barré syndrome); and local signs and symptoms at the injection site, such as pain and swelling, itching, redness, swollen lymph nodes, cutaneous rash, or peripheral reactions (eg, Raynaud's syndrome), as well as anaphylactic reactions requiring emergency hospital access.[15,18]

Delirium Assessment

As part of the GeroCovid Vax Consortium, 2 web meetings were conducted with all the managers of the LTCFs to ensure proper detection of delirium. During these meetings, we aimed to train LTCF managers to enhance their delirium knowledge and increase their capability to detect delirium in line with the current diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition of the American Psychiatric Association (DSM-5). Incident delirium was clinically assessed and systematically collected daily for 7 days following each vaccination dose following the GeroCovid Vax study protocol to ensure an observation time that could accurately detect delirium incidence.[19,20] To enhance the sensitivity in detecting delirium within the study sample, we used an inclusive approach considering all potential keywords associated with delirium, as per a previously published methodology,[19] and aligned with the previously mentioned DSM-5 criteria for the definition of delirium, which encompasses clinically identifying characteristics such as confusion, disorientation, altered mental status, delirium, agitation, inappropriate behavior, mental status change, inattention, hallucinations, and lethargy.[21-23] In the context of this study, patients were classified as delirious if they displayed at least 1 of the following features during any visit following each vaccination: delirium, confusion, and/or insomnia/restlessness. Subsequently, a binary variable indicating the presence or absence of delirium "at any time" was established as the outcome variable. Using a similar methodology, a binary variable for the presence or absence of delirium after each vaccination dose was created to assess the incidence of delirium.

Data Analysis

Descriptive statistics were used to summarize key demographic and clinical baseline characteristics of the study cohort according to delirium status. Continuous variables were expressed as means and SDs, whereas categorical variables were presented as absolute and relative frequencies. Differences between participants in relation to the presence or absence of delirium were evaluated using *t* test or Wilcoxon test for continuous variables and the χ^2 test or Fisher test for categorical variables when appropriate.

After excluding data points for a subset of variables with >5% missing data within the total sample (n = 3280), the analysis of the primary outcome was conducted on a subset of participants (n = 2521). The incidence of delirium after each vaccination dose was assessed as the number of cases per vaccinated patients, and the data for the incidence of delirium were visually represented as a bar chart. To identify factors associated with delirium following any of the 3 doses of SARS-CoV-2 vaccination among older adults living in LTCFs, we performed both univariable and multivariable logistic regression analyses using delirum at "any time" as the outcome variable as previously described (see Delirium Assessment section). Results of the multivariable regression are presented as a forest plot, displaying odds ratio (ORs) and 95% CIs. A significance level of $P < .05$ was considered, with false discovery rate (FDR) adjustment at 5% for multiple comparisons. Collinearity was assessed through graphical visualization of correlation matrices and variance inflation factor (VIF), with no evidence of severe collinearity detected (VIF < 10).

Network Analysis

A classical non-Bayesian network analysis was conducted to elucidate the connections between recorded post-vaccination symptoms and delirium within the study cohort. This analysis aimed to identify the relationships and interactions among symptoms to better understand their potential roles in the development of delirium. We used a standard correlation method to construct the network, normalizing the data to ensure comparability across different symptoms. A tuning parameter set at 0.5 was applied to balance network sparsity and connectivity, ensuring that the network was neither too dense nor too sparse, which could obscure meaningful relationships or highlight spurious connections. The resulting weights matrix quantified the strength of correlations between each pair of symptoms, where positive values indicated positive correlations and negative values indicated negative correlations.

These correlations were visually represented in a network plot, allowing for intuitive interpretation of the relationships between symptoms. Centrality measures were computed to assess the importance of each symptom within the network.

- Betweenness Centrality: This measure indicated how often a symptom appeared on the shortest paths between other symptoms, highlighting its role as a bridge or connector within the network.
- Closeness Centrality: This measure reflected how quickly information could spread from a symptom to all other symptoms in the network, indicating the symptom's overall reach.
- Strength Centrality: This measure represented the sum of the absolute values of the weights of the edges connected to a symptom, indicating the symptom's overall involvement in the network.

These measures provided a comprehensive understanding of the network dynamics and the potential impact of individual symptoms on the development of delirium.

Data analysis and graphics were performed in the R statistical environment (version 4.3.2) using the Tidyverse and sjPlot packages; the network analysis was performed on JASP (version 0.017.1.0).

Results

Table 1 summarizes the baseline characteristics of the study sample. The mean age of the 2521 participants was 83.10 years (SD ± 9.21), and 1784 (70.7%) were women. Cognitive disorders affected more than two-thirds (67.0%) of the study population, with 12.0% having a history of chronic kidney disease and 11.7% of arterial hypertension. Antipsychotics were used by 40.9% of participants,

followed by antidepressants (36.5%) and anxiolytics (20.4%). Only 3.3% of participants took antidementia medications. In the study sample, 2357 received the first vaccine dose, 1507 received the second dose, and 1178 received a booster dose. A total of 145 patients (5.75%) experienced delirium after any of the vaccination doses (first dose, second dose, or booster dose). Delirium occurred in 3.5% of cases after the first dose, 1.6% after the second one, and 1.5% after the booster dose (Supplementary Figure 1). Summary of principal type of LTCFs in relation to delirium incidence and baseline characteristics of excluded data are available in Supplementary Tables 1 and 2.

Patients with delirium were significantly older than non-delirious individuals [mean age 85.52 (7.03) vs 82.96 (9.31), $P < .001$], with a higher prevalence of cognitive disorders [83.4% vs 66.0%] and were more frequently frail [34.5% vs 17.7%].

Physical frailty and cognitive impairment significantly predicted delirium [respectively, OR, 2.05; 95% CI, 1.40–2.97; $P = .003$; OR, 1.70; 95% CI, 1.08–2.77; $P = .050$] after FDR correction for multiple testing. The use of antipsychotics and antidepressants was also significantly associated with the onset of delirium after any vaccination dose [respectively, OR, 1.75; 95% CI, 1.22–2.51; $P = .009$; OR, 1.77; 95% CI, 1.25–2.52; $P = .008$] (Figure 1 and Supplementary Table 3). Conversely, the presence of Parkinson's disease showed a nonsignificant effect on delirium after FDR adjustment [OR, 2.01; 95% CI, 1.00–3.70; $P = .08$], while the mobility level seemed not to be related to delirium. VIF values and variable correlations plots are available in Supplementary Table 4 and Supplementary Figures 2 and 3.

In parallel, the network analysis revealed several interconnected pathways among post-vaccination symptoms. Notably, a moderate to strong positive association was identified between experiencing anorexia or chills and the occurrence of delirium (respectively, coefficient = 0.46 and 0.23) Conversely, the network analysis indicated weak associations between delirium and fever (coefficient = 0.136) and dyspnea (coefficient = −0.126) (Figure 2, Supplementary Table 5, and Supplementary Figure 4).

Discussion

This study presents data from the Italian GeroCovid Vax study, focusing on the potential associations between delirium incidence and SARS-CoV-2 vaccinations in older adults living in LTCFs. The findings

Table 1
General Characteristics, Comorbidities, and Medications of the Study Population, According to Any Delirium Incidence After Any Vaccination

Participant Characteristics, Overall and by Delirium Status				
Variables	All Participants N = 2521*	Absence of Delirium n = 2376 (94.2%)*	Presence of Delirium n = 145 (5.8%)*	*P* Value†
Age, y	83.10 (9.21)	82.96 (9.31)	85.52 (7.03)	**<.001**
Women, n (%)	1784 (70.7)	1679 (70.6)	105 (72.4)	.72
Comorbidities				
Diabetes	198 (7.9)	187 (7.9)	11 (7.6)	1.00
Atrial fibrillation	36 (1.4)	32 (1.3)	4 (2.8)	.14
Arterial hypertension	295 (11.7)	286 (12.0)	9 (6.2)	**.047**
Renal insufficiency	293 (12.0)	270 (11.8)	23 (15.9)	.18
Obesity	41 (1.6)	40 (1.7)	1 (0.7)	.72
Respiratory diseases	117 (4.6)	110 (4.6)	7 (4.8)	.83
Current smoker	140 (5.6)	134 (5.7)	6 (4.3)	.24
Cancer	255 (10.5)	233 (10.2)	22 (15.2)	.07
Alcohol use	90 (3.6)	84 (3.6)	6 (4.3)	**<.001**
Liver diseases	141 (5.8)	131 (5.7)	10 (6.9)	.68
Cognitive disorders	1689 (67.0)	1568 (66.0)	121 (83.4)	**<.001**
Parkinson's disease	119 (4.7)	107 (4.5)	12 (8.3)	.06
Depression	211 (8.4)	203 (8.5)	8 (5.5)	.26
Anxiety	69 (2.7)	62 (2.6)	7 (4.8)	.18
Psychiatric diseases	215 (8.5)	209 (8.8)	6 (4.1)	.07
Epilepsy	77 (3.1)	75 (3.2)	2 (1.4)	.31
Thyroid diseases	223 (8.8)	205 (8.6)	18 (12.4)	.15
Osteoporosis	220 (8.7)	199 (8.4)	21 (14.5)	**.017**
Osteoarthritis	139 (5.5)	136 (5.7)	3 (2.1)	.09
Medications				
Muscle relaxants	32 (1.3)	30 (1.3)	2 (1.4)	.70
Pain medications	326 (12.9)	299 (12.6)	27 (18.6)	**.048**
Antiepileptics	494 (19.6)	461 (19.4)	33 (22.8)	.37
Antiparkinsonian medications	225 (8.9)	205 (8.6)	20 (13.8)	**.049**
Antipsychotics	1030 (40.9)	953 (40.1)	77 (53.1)	**.003**
Anxiolytics	514 (20.4)	485 (20.4)	29 (20.0)	.98
Hypnotics	244 (9.7)	228 (9.6)	16 (11.0)	.67
Antidepressants	921 (36.5)	842 (35.4)	79 (54.5)	**<.001**
Antidementia medications	83 (3.3)	78 (3.3)	5 (3.4)	.81
Physical performance				
Physical frailty	470 (18.6)	420 (17.7)	50 (34.5)	**<.001**
Mobility level				
Can walk independently or with walking aid (cane or walker)	349 (14.3)	326 (14.1)	23 (16.0)	**.026**
Mobility is possible only with a wheelchair	969 (39.6)	899 (39.0)	70 (48.6)	
Mobility completely dependent on others, lying in bed at all times or most of the times	1130 (46.2)	1079 (46.8)	51 (35.4)	
Type of vaccine				.76
BNT162b2	2306 (91.5)	2172 (91.4)	134 (92.4)	
mRNA-1273	215 (8.5)	204 (8.6)	11 (7.6)	

mRNA, BioNTech RNA Pharmaceuticals e Pfizer; mRNA, National Institute of Allergy and Infectious Diseases e Moderna.
*Mean (SD); n (%).
†Welch 2-Sample *t* test; Pearson's χ^2 test or Fisher test. *P* values <.05 are in bold.

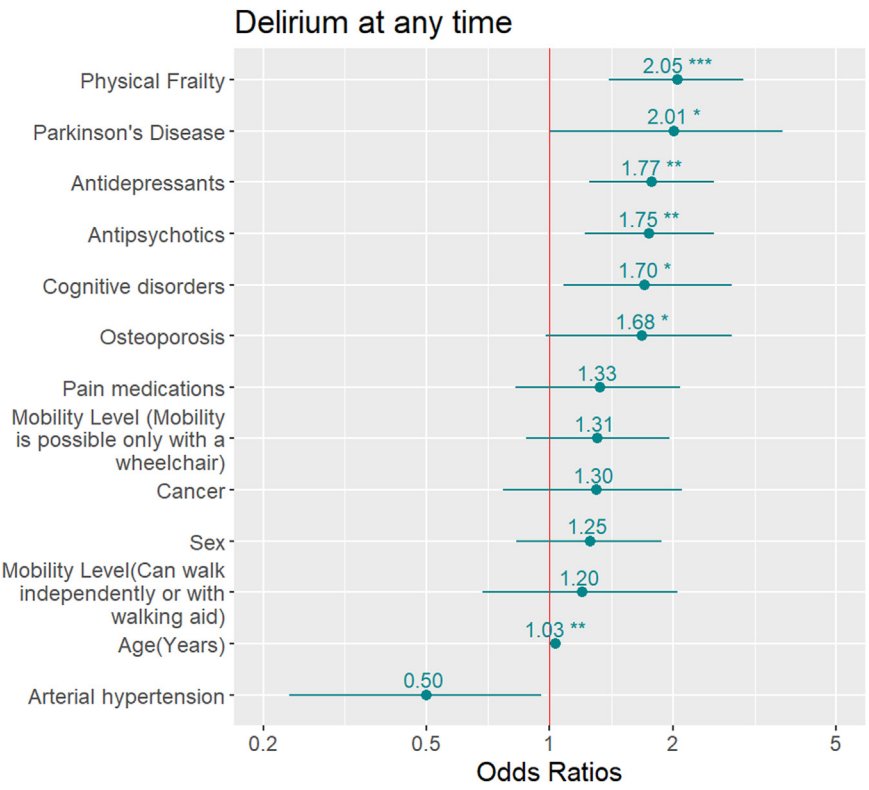

Fig. 1. The forest plot visually represents the results obtained from a multivariable logistic regression model. It offers insight into the likelihood of delirium occurrence during any visit following vaccination, providing a comprehensive understanding of the impact of vaccination on this specific symptom.

indicate a low risk of delirium following SARS-CoV-2 vaccination, with a progressive decrease in incidence dose by dose over time. After adjustment for demographic and clinical confounders, frailty syndrome, cognitive impairment, and the use of antipsychotic and antidepressant medications emerged as predictors of delirium onset in LTCF residents after SARS-CoV-2 vaccination. Anorexia and chills were identified as the symptoms most strongly associated with post-vaccination delirium, whereas weaker correlations were observed

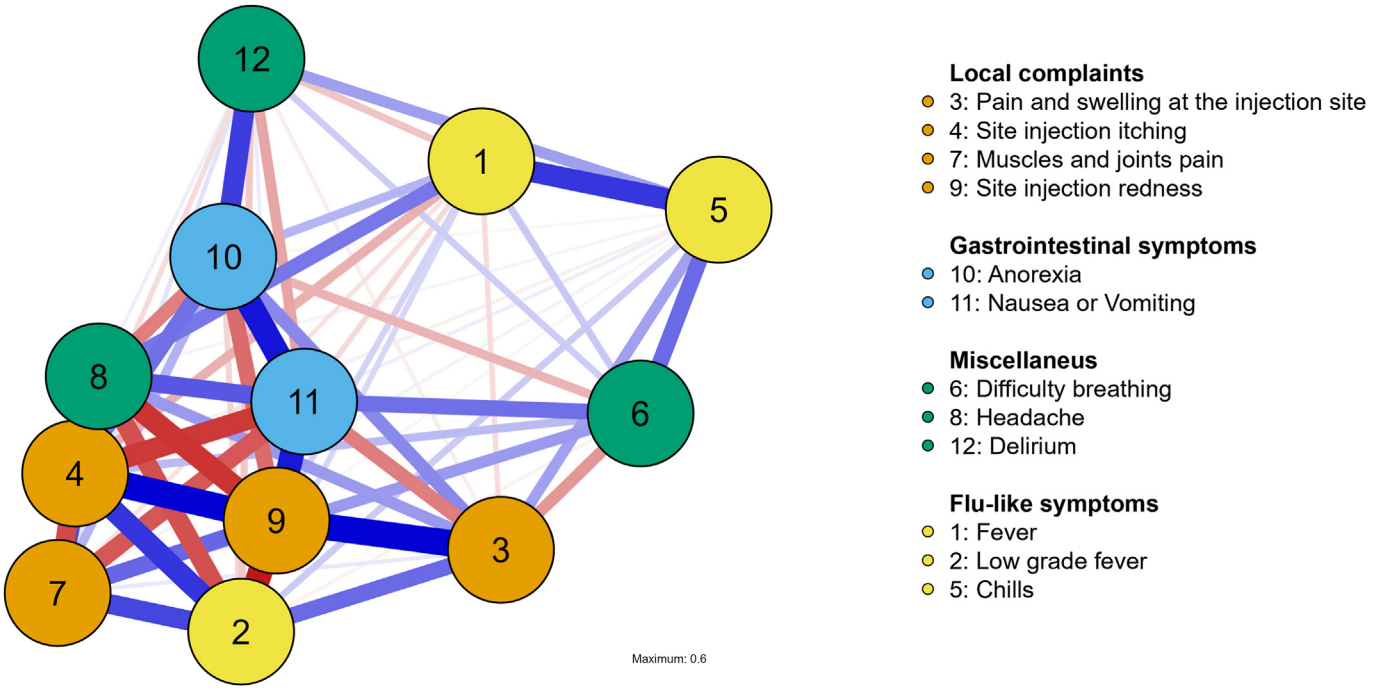

Fig. 2. In this diagram, we present the intricate network structure of interconnected pathways associated with post-vaccination symptoms. By visualizing these pathways, we gain a deeper understanding of the complex interactions and relationships among different symptoms, contributing to our comprehension of the post-vaccination symptomatology.

with fever, dyspnea, and muscle pain. Collectively, these results highlight the safety of SARS-CoV-2 vaccines in relation to confusional states and delirium, particularly in the context of very old and frail individuals.

The prevalence of delirium in LTCFs is subject to conflicting data. A recent study in Danish LTCFs reported a 60% incidence of delirium following acute conditions in older residents. Furthermore, in a previous study from our study group, delirium emerged as the most common atypical sign of SARS-CoV-2 infection in older LTCF residents, yielding a 41.2% prevalence.[3] Thus, the incidence of delirium post vaccine seems favorable compared with the risk of delirium (and other adverse effects) post SARS-CoV-2 infection.

Although older residents in European LTCFs were among the first to receive vaccine doses, phase II and phase III studies of SARS-CoV-2 vaccines included a minimal proportion of older adults. In the Moderna Phase III study, only 0.2% of participants were LTCF residents, explaining the lack of assessment for delirium and confusional states in the trial.[24] Similarly, neither Pfizer's nor Johnson & Johnson's phase II and phase III studies described these symptoms.[25] However, delirium has been documented in the Vaccine Adverse Event Reporting System (VAERS) as an adverse reaction to COVID-19 vaccines.[26] In a prior case series conducted in an American Nursing Home, 7.5% of the study population experienced delirium the day after receiving the vaccine, with all cases being reversible.[12] In our study, we observed a comparable incidence of delirium, and it was independently linked to pre-existing cognitive impairment, consistent with previous reports highlighting dementia as a strong risk factor for delirium in LTCF residents.[27,28] As anticipated, the use of antipsychotics exhibited an association with delirium, persisting even after adjusting for frailty. Notably, antipsychotic medications have a well-established deliriogenic effect and are often inappropriately prescribed in the presence of behavioural symptoms related to dementia, especially in LTCF, such that receipt of antipsychotic medication may be a marker of non-cognitive symptoms of dementia, and hence a propensity to delirium.[28] Furthermore, our findings outline the pivotal role of frailty assessment in predicting adverse outcomes, particularly delirium. Irrespective of mobility status and a history of dementia, frailty emerged as a robust driver for delirium after SARS-CoV-2 vaccination.[29] Many of these factors have been identified as predictors of negative outcomes after SARS-CoV-2 infection[29]; therefore, given the efficacy and safety of the vaccine, promptly recognizing them is essential in implementing preventive strategies to ensure a successful vaccination campaign and management of post-vaccination symptoms. For instance, LTCF residents exhibiting these risk factors may benefit from a standardized approach aimed at reducing delirium occurrence, encompassing interventions such as physical exercise, music therapy, avoidance of physical restraints, and ensuring adequate bed rest.[30] The network analysis revealed pathways connecting diverse post-SARS-CoV-2 vaccination symptoms. Remarkably, anorexia surfaced as the post-vaccination symptom exhibiting the strongest correlation with delirium. This correlation aligns seamlessly with the "aberrant stress response" theory, stemming from dysregulated adaptive systemic and central nervous systems (CNS) reactions to stressors.[31] Thus, symptoms like diminished appetite and fatigue may represent the aberrant stress response to the systemic inflammation caused by the vaccination. This constellation of symptoms, termed sickness behavior, may be dysregulated in older frail individuals, serving as an adaptive mechanism to conserve energy and minimize exposure to escalating infections. This concept is reinforced by the observation that frail patients often exhibiting predominant atypical symptoms, also displayed a low incidence of inflammation-related side effects triggered by immunization.[32,33]

Furthermore, considering delirium as a nonspecific manifestation of illness, stronger associations with alternative conditions caused by health care–associated infections (HAI) in LTCFs (such as fever or dyspnea) would be anticipated. These insights contribute to our understanding of the complex interplay among vaccination, physiological responses, and the nuanced manifestations of adverse effects in distinct patient populations. The weaker connections with fever and dyspnea suggest that the link between delirium and vaccination is more specific.

This study acknowledges limitations such as the lack of validated delirium recognition tools and reliance on a questionnaire filled out by LTCF personnel, potentially underestimating delirium and hindering subtype distinction. As a fact, despite conducting web meetings to enhance delirium detection among LTCF and managers using DSM-V criteria, the variability in facility sizes, types and understaffing during the COVID-19 pandemic made it impractical to implement a standardized assessment tool like the 4AT. This likely led to underdetection of delirium, although standardized keywords in data collection may have improved accuracy. Furthermore, not all facilities systematically assessed for previous COVID-19 infections before vaccination, which could introduce potential bias in the diagnosis of delirium.

In addition, not only early-stage dementia might have been undetected thus impacting delirium recognition, but also the lack of data on disease severity might have introduced further confounding. The absence of data concerning the severity of underlying diseases, especially in the case of c Retrospective methodology using clinical chart keywords was used to enhance the findings' robustness. Despite declining incidence rates with repeated doses supporting delirium detection validity, residual confounding due to age cannot be entirely ruled out, consistently with evidence underlying age as a predominantly risk factor for delirium.[34] The predominantly white resident population limits generalizability. Future studies should incorporate validated assessment tools, diverse cohorts, and prospective methodologies to refine understanding. Nevertheless, this multicenter, national study provides comprehensive insights into SARS-CoV-2 vaccination outcomes among older adults in LTCFs, highlighting predictors such as frailty, cognitive impairment, and medication use. Despite limitations, the standardized approach enhances delirium recognition reliability, addressing critical research gaps and informing future vaccination strategies and patient care for this vulnerable population.

Conclusions and Implications

This study suggests that the anti-SARS-CoV-2 vaccination is safe in terms of delirium onset in older adults living in LTCFs. Nonetheless, our findings underlie that principal predisposing factors of delirium in older patients are frailty syndrome, cognitive impairment, and the use of antipsychotics and antidepressant medications. The value of our work lies in the representativeness of the sample, adequately encompassing the older adult population. We hope that our research can serve as inspiration for future studies focused on implementing strategies to enhance vaccination adherence, thereby ensuring successful aging for the most vulnerable populations.

Disclosures

The authors declare no conflicts of interest.

Acknowledgments

We would like to extend our heartfelt gratitude to all the patients and staff members of the LTCFs for their participation and cooperation. Special thanks to the Delirium SIG of the EuGMS and all the researchers involved in the GeroCovid Vax Study.

Supplementary Data

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.jamda.2024.105251.

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