

Delirium as a Presenting Symptom of COVID-19

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Background: Delirium is a common neurologic manifestation of coronavirus disease 2019 (COVID-19) in older adults who present to the emergency department (ED).

Objective: To investigate clinical characteristics associated with delirium as a presenting symptom of COVID-19 in older adults and develop a logistic regression to predict the likelihood of delirium.

Method: We compared clinical characteristics in an age- and gender-matched sample of 68 delirious individuals with 68 nondelirious individuals ($M_{age} = 78$) who presented to the ED with COVID-19.

Results: The delirious group was more likely to have neurologic, psychiatric, and cardiovascular comorbidities; a prior history of delirium; and deliriogenic medications in their medication list. They were less likely to present with respiratory symptoms and more likely to present with sepsis, hypoxia, higher heart rate, and higher sodium. The delirious group had higher mortality (51%) than the nondelirious group (32%). Delirium developed within an average of 2 days of initial COVID-19 symptom onset, with symptom onset to ED within an average of 4 days and symptom onset to death within an average of 11 days. Logistic regression based on five delirium predictors correctly predicted 80% of those with delirium (75% sensitivity at 86% specificity).

Conclusion: Our results are largely consistent with prior studies and suggest that delirium is a common, early occurring, and lethal manifestation of COVID-19 in older adults presenting to the ED, in most cases causing acute on chronic neurocognitive dysfunction strongly influenced by inflammatory and hypoxic-ischemic mechanisms.

Key Words: COVID-19, delirium, neurology, psychiatry, neuropsychology

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COVID-19=coronavirus disease 2019. **ED**=emergency department. **SARS-CoV-2**=severe acute respiratory syndrome coronavirus 2.

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease it causes, coronavirus disease 2019 (COVID-19), is associated with neurologic manifestations such as delirium, dizziness, headache, myalgia, hyposmia, hypogeusia, seizure, and stroke (Agarwal et al, 2021; Chen et al, 2020; Mao et al, 2020). Delirium is the most common neurologic manifestation of COVID-19 in hospitalized older adults and is associated with high mortality (Kennedy et al, 2020; Mendes et al, 2020; Pranata et al, 2021; Tyson et al, 2020). Studies have investigated the development of delirium over the course of hospitalization, such as when in the intensive care unit and/or removed from a ventilator (Garcez et al, 2020; Helms et al, 2020a, 2020b), and delirium as a presenting symptom of COVID-19 in the emergency department (ED) (Kennedy et al, 2020; Tyson et al, 2020, 2021).

Delirium due to COVID-19 shares many features of delirium due to other etiologies. Factors strongly associated with delirium due to other etiologies include dementia; older age; infection; comorbid illness; severity of medical illness; diminished activities of daily living; immobility; sensory impairments; electrolyte imbalance; malnutrition; history of alcohol abuse; and “high-risk” medications such as anticholinergics, benzodiazepines, and opioids (Ahmed et al, 2014; Han et al, 2010). Factors strongly associated with delirium as a presenting symptom of COVID-19 include preexisting cognitive impairment and dementia, older age, assisted living or nursing home residence, neurologic and cardiovascular comorbidities, prior use of psychoactive medication, vision impairment, hearing impairment, and less typical symptoms of COVID-19 (Kennedy et al, 2020; Mendes et al, 2020; Poloni et al, 2020; Tyson et al, 2020, 2021).

In this study, we build upon previous work describing delirium due to other etiologies and add to the growing literature on delirium due to COVID-19 by further investigating associated factors and developing a logistic regression to predict the likelihood of delirium as a presenting symptom of COVID-19 in the ED.

METHOD

Participants

We collected data through a clinical chart review of 516 consecutive individuals with SARS-CoV-2 infection seen in the ED between February 20, 2020, and July 8, 2020, at EvergreenHealth Medical Center—the first hospital with reported SARS-CoV-2 cases in the United States. EvergreenHealth Medical Center is a public

hospital serving nearly 850,000 people in the King and Snohomish counties of Washington State. It has 318 hospital beds, including 20 beds in the intensive care unit and 15 beds in the hospice care center. The hospital experienced 47,643 ED visits and 13,819 acute care admissions in 2020.

The comparison group consisted of the first 68 individuals matching the age and gender of the delirious sample who presented to the ED during the same data collection period. Both groups had SARS-CoV-2 infection confirmed by polymerase chain reaction testing of a nasopharyngeal sample.

The study protocol was approved by the institutional review board and ethics committee of the EvergreenHealth Medical Center of Kirkland, Washington, and was performed according to the ethical guidelines of the Declaration of Helsinki and its later amendments.

Materials

We collected data regarding relevant demographic characteristics, medical history, medications, presenting signs and symptoms of COVID-19, vital signs and available laboratory findings in the ED, hospitalization characteristics, and individual outcomes. Presenting signs and symptoms were reported by the individuals themselves, family members, care partners, nursing staff, emergency responders, and physicians. Determination of delirious medications was based on the Beers criteria for potentially inappropriate use in older adults (2019 American Geriatrics Society Beers Criteria Update Expert Panel, 2019) and included documented daily use of anticholinergics, antiepileptic drugs, antihistamines, antipsychotics, benzodiazepines, and/or opioids. We gathered additional information regarding baseline mental status, hospitalization characteristics, and individual outcomes from outpatient office visit notes, nursing and progress notes, consultation reports, discharge summaries, and death reports.

A neurologist (P.A.) and neuropsychologist (B.T.) independently reviewed all patient medical records and cross-referenced presenting symptoms. We established the diagnosis of delirium using the Chart-based Delirium Identification Instrument (Inouye et al, 2005), which is a well-validated method for identifying the presence of delirium based on evidence in the medical record. Delirium was defined as acute disturbance of attention and awareness representing a decline from baseline mental status. We considered key words such as altered mental status, confusion, delirium, disorientation, encephalopathy, decreased level of consciousness, and impaired consciousness. We excluded individuals if (a) their mental status changes did not clearly represent a decline from a previously higher baseline, (b) they were comatose at hospital admission, (c) their medical records lacked sufficient data to substantiate the diagnosis, and/or (d) there was a lack of consensus between P.A. and B.T.

Statistical Analysis

Descriptive statistics (M, SD, percentage, LR, OR, and 95% CI) were computed for relevant variables. The

statistical significance of between-group differences was determined using independent *t* tests (two-tailed) and χ^2 . Effect size estimates were expressed in Cohen's *d*. A logistic regression classifier was used to predict delirium as a presenting symptom of COVID-19 with the addition of lasso regularization to avoid overfitting, as our data comprised a high-dimensional set of clinical metrics. We used MATLAB's Statistics and Machine Learning Toolbox function, *lassoglm*.

The clinical predictors used in our model, motivated by our univariate group comparison, included the use of deliriogenic medication, history of dementia, history of stroke, prior delirium, and assisted versus independent living residence. Per convention, we randomly partitioned our data into 80:20 training:test sets. We fit our regression on the training set >100 values of the regularization parameter lambda and evaluated predictions exclusively on the test set. We repeated this process 100 times to generate CIs for model performance, with our data being randomly partitioned each iteration. Our results were robust to changes in the cross-validation partition, the span of our lambda regularization parameters, and the number of repeat modeling iterations.

RESULTS

Participants

Demographic information and medical history are provided in Table 1. Of the 516 individuals with COVID-19 who were seen in the ED during the study period, 100 (19%) demonstrated potential evidence of acute cognitive disturbance, but only 68 (13%) met our diagnostic inclusion criteria for delirium. Of the 136 individuals we included in our study, the majority were Caucasian/White (85%), with slightly more females (54%) than males (46%) and an average age of 78 years (range 53–99). There were no between-group differences in age, gender, or ethnicity.

Individuals with delirium were more likely than individuals without delirium to come from assisted living facilities or nursing homes (72%) compared with independent living residences (28%). Individuals with delirium also had higher rates of neurologic comorbidities, particularly dementia and stroke, and psychiatric comorbidities. All dementia subtypes were more common in the delirious group. There were no specific psychiatric comorbidities differences between the two groups, but all five individuals with schizophrenia presented with delirium, which approached significance. Cardiovascular disease was the only medical comorbidity more common in the delirious group.

With respect to other predisposing factors, individuals with delirium were more likely to have a prior history of delirium (49%) than individuals without delirium (13%). Individuals with delirium were also more likely to have at least one deliriogenic medication listed in their medication list and were taking more deliriogenic medications (M = 1.24, SD = 1.21) than the individuals without delirium (M = 0.56, SD = 0.85): $t_{134} = -3.76$, $P \leq 0.001$. Baseline hearing and visual impairments were more

TABLE 1. Demographic Information and Medical History

Demographic/Clinical History	M (SD)	With Delirium	Without Delirium	<i>t</i>	<i>P</i>
Age	78.25 (10.73)	78.65 (11.01)	77.85 (10.63)	-0.428	0.669
Gender	n (%)			χ^2	<i>P</i>
Female/male	74/62 (54/46)	37/31	37/31	0.00	1.00
Ethnicity					
Caucasian/White	116 (85)	57	59	0.06	0.81
Asian/Pacific Islander	10 (7)	5	5	0.00	1.00
Hispanic/Latinx	5 (4)	3	2	0.00	1.00
African American/Black	2 (1)	1	1	0.00	1.00
Unknown/unavailable	3 (2)	2	1	0.00	1.00
Living situation					
Assisted/independent	64/72 (47/53)	19/49	45/23	18.45	<0.001***
Medical comorbidities	126 (93)	66	60	2.7	0.1
Hypertension	92 (68)	45	47	0.03	0.855
Cardiovascular disease	75 (55)	44	31	4.28	0.039*
Diabetes	47 (35)	23	24	0.00	1.00
Chronic lung disease	34 (25)	16	18	0.04	0.843
Chronic kidney disease	34 (25)	18	16	0.04	0.843
Obesity	30 (22)	15	15	0.00	1.00
Cancer	29 (21)	15	14	0.00	1.00
Obstructive sleep apnea	23 (17)	11	12	0.00	1.00
Liver disease	11 (8)	4	7	0.40	0.529
Neurologic comorbidities	72 (53)	58	14	54.57	<0.001***
Dementia	49 (36)	44	5	46.07	<0.001***
Stroke	25 (18)	20	5	9.60	0.002**
Brain tumor	5 (4)	4	1	0.83	0.366
Parkinson's disease	4 (3)	3	1	0.26	0.619
Seizure disorder	3 (2)	3	0	1.37	0.244
Multiple sclerosis	2 (1)	2	0	0.51	0.496
Psychiatric comorbidities	74 (54)	45	29	6.67	0.01*
Depression	55 (40)	32	23	1.95	0.162
Anxiety	30 (22)	16	14	0.04	0.836
Insomnia	17 (13)	12	5	2.42	0.120
Opioid use disorder	12 (9)	9	3	2.29	0.131
Alcohol use disorder	8 (6)	5	3	0.13	0.718
Bipolar disorder	8 (6)	6	2	1.20	0.274
Schizophrenia	5 (4)	5	0	3.32	0.058
Other predisposing factors					
Prior delirium	42 (31)	33	9	17.36	<0.001***
Deliriogenic medications	68 (50)	44	24	10.62	0.001**
Baseline hearing impairment	17 (13)	11	6	1.08	0.300
Baseline visual impairment	7 (5)	5	2	0.60	0.438

*Significant at $P < 0.05$.
**Significant at $P < 0.01$.
***Significant at $P < 0.001$.

common in the delirious group but were not significantly different between groups.

Presenting signs and symptoms are provided in Table 2. Individuals with delirium were less likely than

individuals without delirium to have respiratory symptoms, particularly cough. They were also less likely to report diarrhea or myalgia, but at a marginally significant level. Three individuals presented to the ED

TABLE 2. Presenting Signs and Symptoms

Signs and Symptoms	n (%)	With Delirium	Without Delirium	χ^2	P
Respiratory symptoms	110 (81)	49	61	5.75	0.016*
Cough	93 (68)	39	54	6.66	0.010*
Shortness of breath	81 (60)	35	46	3.05	0.081
Complaints of fever	93 (68)	46	47	0.00	1.00
Fever $\geq 100.4^\circ\text{F}$ in ED	27 (20)	18	9	2.82	0.093
Weakness/fatigue	72 (53)	31	41	2.39	0.122
Anorexia	45 (33)	20	25	0.53	0.466
Diarrhea	39 (29)	14	25	3.60	0.058
Myalgia	21 (15)	6	15	3.60	0.058
Dizziness	20 (15)	8	12	0.53	0.468
Balance difficulties/falls	19 (14)	12	7	0.98	0.322
Headache	17 (13)	5	12	2.42	0.120
Nausea/vomiting	12 (9)	3	9	2.29	0.131
Hypogeusia/hyposmia	3 (3)	0	3	3.07	0.244
Stroke	3 (3)	3	0	3.07	0.244
Seizure	1 (1)	1	0	0.00	1.00

*Significant at $P < 0.05$.

ED = emergency department.

with ischemic stroke, all of whom had a prior history of stroke. One additional individual experienced a transient ischemic attack 1 week before testing positive for COVID-19, and another experienced a hemorrhagic stroke while hospitalized. One individual presented with nonconvulsive status epilepticus without a prior history of seizure, and one individual displayed suicidal and homicidal behavior. No delirious individuals complained of hypogeusia or hyposmia.

Vital signs, laboratory findings, acute illness-related factors, and hospitalization characteristics are reported in Table 3. Individuals with delirium had higher heart rates and higher sodium compared to individuals without delirium. In the ED, 46% of individuals with delirium had acute respiratory distress syndrome, 34% were dehydrated/malnourished, 31% had hypoxia, 28% had sepsis, 25% had acute kidney injury, and 18% had multiple organ dysfunction. Individuals with delirium were more likely to have hypoxia (oxygen saturation $<90\%$) and sepsis. There were no between-group differences in admission to critical care or use of mechanical ventilation.

Delirium developed within an average of 2 days of initial COVID-19 symptom onset ($M = 1.53$, $SD = 0.97$). These individuals were taken to the ED within an average of 4 days of initial symptom onset ($M = 3.57$, $SD = 3.25$), which was significantly faster than individuals without delirium ($M = 6.7$, $SD = 4.57$): $t_{130} = 4.51$, $P \leq 0.001$. Symptom onset to death occurred within an average of 11 days in the delirious group ($M = 10.74$, $SD = 9.01$, range 1–38) and within an average of 13 days in the nondelirious group ($M = 12.84$, $SD = 6.44$, range 3–27): $t_{134} = 0.90$, $P = 0.374$. A total of 57 study participants died, 35 with delirium and 22 without. Mortality included both in-hospital (41) and hospice (16) mortality within 3 months of initial hospitalization date.

Individuals with delirium had higher mortality (51%) than individuals without delirium (32%): $LR = 1.59$, $\chi^2_{(1)} = 4.34$, $P = 0.037$.

In our sample of 68 individuals with delirium due to COVID-19 in the ED, a hypoactive delirium was seen in 62% and a hyperactive delirium was seen in 16%. A mixed level of activity was documented in 22%. Twenty individuals (29%) demonstrated agitation, and five (6%) experienced hallucinations. Delirium without respiratory symptoms was present in 18 individuals (26%), and delirium as the only presenting symptom was seen in six individuals (9%).

All six individuals with delirium as the only presenting symptom of COVID-19 had a prior history of delirium, four had dementia, four had a history of stroke, and two had schizophrenia. These individuals were approximately the same age as the rest of the delirium sample ($M = 75.17$, $SD = 12.13$, range 64–91) and had a comparable mortality rate (50%). Only one of these individuals developed respiratory symptoms after admission. Of the three individuals who died, one had a history of brain metastases, dementia, and end-stage renal disease and developed critical hypoglycemia after missing dialysis; one had a history of vascular dementia and suffered a hemorrhagic stroke while hospitalized; and one had a history of schizophrenia, chronic kidney disease, and liver disease and developed septic shock and multiple organ failure. Symptom onset to death was faster in those with delirium as the only presenting symptom of COVID-19 ($M = 3.67$, $SD = 2.52$) compared with those presenting with delirium and other symptoms ($M = 11.4$, $SD = 9.13$), but given the limited sample size, this was not statistically significant, $t_{33} = 1.45$, $P = 0.154$.

Our logistic regression contained the following binary predictors (listed with their respective OR and [95% CI representing 2 SDs from the sample M]): use of

TABLE 3. Vital Signs, Laboratory Studies, Acute Illness-related Factors, and Hospitalization Characteristics

Vital Signs	M (SD)	With Delirium	Without Delirium	<i>t</i>	<i>P</i>	<i>d</i>
Temperature °F	99.27 (1.58)	99.39 (1.89)	99.14 (1.17)	-0.959	0.340	—
Temperature °C	37.38 (0.88)	37.45 (1.06)	37.29 (0.65)	-1.02	0.309	—
Heart rate	88.35 (22.39)	93.53 (25.69)	83.16 (17.18)	-2.76	0.007**	0.47
Respiratory rate	22.74 (9.02)	24.12 (11.29)	21.34 (5.66)	-1.77	0.080	—
Blood pressure systolic	130.71 (23.78)	127.12 (25.91)	134.31 (20.99)	1.78	0.078	—
Blood pressure diastolic	71.89 (13.67)	71.39 (15.98)	72.38 (10.99)	0.419	0.676	—
Oxygen saturation	92.68 (6.73)	92.06 (8.07)	93.31 (5.04)	1.08	0.281	—
Laboratory studies, measurement						
White blood cell, / μ L	8.42 (5.02)	8.62 (4.75)	8.22 (5.29)	-0.459	0.647	—
Hemoglobin, g/DL	12.16 (2.17)	11.93 (1.86)	12.39 (2.43)	1.25	0.212	—
Hematocrit, %	37.84 (6.25)	37.31 (5.21)	38.36 (7.14)	0.981	0.329	—
Absolute platelet, $10^3/\mu$ L	214.66 (101.15)	209.41 (96.81)	219.91 (105.77)	0.604	0.547	—
Sodium, mmol/L	136.79 (6.24)	138.12 (6.96)	135.46 (5.14)	-2.53	0.012*	0.43
Potassium, mmol/L	4.08 (0.61)	4.09 (0.68)	4.06 (0.54)	-0.339	0.735	—
Chloride, mEq/L	98.21 (6.36)	99.27 (7.13)	97.15 (5.31)	-1.94	0.055	—
Carbon dioxide, mEq/L	23.99 (3.79)	24.22 (4.59)	23.74 (2.78)	-0.733	0.465	—
Blood urea nitrogen, mmol/L	26.82 (16.53)	28.89 (17.91)	24.75 (14.86)	-1.47	0.144	—
Creatinine, mg/dL	1.29 (1.26)	1.31 (1.24)	1.27 (1.29)	-0.176	0.861	—
Glucose, mmol/L	139.19 (64.33)	140.89 (67.58)	137.42 (61.27)	-0.311	0.756	—
Alanine aminotransferase, U/L	32.79 (37.93)	27.22 (34.5)	38.37 (40.59)	1.66	0.099	—
Aspartate aminotransferase, U/L	48.83 (58.86)	47.06 (64.44)	50.59 (53.15)	0.335	0.738	—
Lactic acid, mmol/L	1.87 (1.22)	2.05 (1.33)	1.58 (0.97)	-1.75	0.084	—
C-reactive protein, mg/DL	9.21 (7.5)	7.91 (6.43)	10.28 (8.21)	1.22	0.227	—
Creatine phosphokinase, U/L	221.27 (339.01)	245.27 (399.74)	190.53 (242.89)	-0.682	0.497	—
Lymphocyte (absolute), $10E3/\mu$ L	1.05 (0.71)	1.04 (0.81)	1.05 (0.61)	0.112	0.911	—
Neutrophil (absolute), $10E3/\mu$ L	6.36 (4.28)	6.69 (4.53)	6.04 (4.05)	-0.825	0.411	—
Acute illness-related factors	n (%)	With Delirium	Without Delirium	χ^2	<i>P</i>	
Acute respiratory distress syndrome	52 (38)	31	21	2.52	0.112	
Dehydration/malnutrition	36 (26)	23	13	3.06	0.080	
Hypoxia, < 90% O ₂	28 (21)	21	7	7.60	0.006**	
Acute kidney injury	26 (19)	17	9	2.33	0.127	
Sepsis	23 (17)	19	4	10.26	0.001**	
Multiple organ dysfunction	17 (13)	12	5	2.42	0.120	
Congestive heart failure	7 (5)	4	3	0.00	1.00	
Acute liver failure	5 (4)	2	3	0.00	1.00	
Hospitalization characteristics	n (%)					
Admission to critical care	51 (38)	30	21	0.231	0.631	
Mechanical ventilation	30 (22)	15	15	0.00	1.00	
Mortality	57 (42)	35	22	4.34	0.037*	

*Significant at $P < 0.05$.**Significant at $P < 0.01$.

deliriogenic medication (OR: 1.65 [1.10]), history of dementia (OR: 11.02 [1.22]), history of stroke (OR: 4.48 [1.35]), prior delirium (OR: 1.49 [1.24]), and assisted versus independent living (OR 1.65 [1.25]). This model performed on testing sets with 75% sensitivity [9%], 86% specificity [8%], and a total accuracy of 80% [6%]. Each of our parameters had P values < 0.05 , which is consistent with our univariate analysis.

DISCUSSION

In our review of 516 consecutive individuals who presented to the ED with COVID-19, 68 individuals (13%) had delirium. The majority of our delirium sample had dementia (65%) and deliriogenic medications in their medication list (65%). Nearly half had a prior history of delirium (49%). All of these factors were significantly more common in the delirious group. The delirious group

was also more likely to have neurologic (dementia and stroke), psychiatric, and cardiovascular comorbidities as well as higher heart rate, higher sodium, and higher rates of hypoxia and sepsis in the ED. Logistic regression based on five delirium predictors (use of deliriogenic medication, history of dementia, history of stroke, prior delirium, and assisted versus independent living) correctly predicted 80% of those with delirium (75% sensitivity at 86% specificity).

The delirious group had higher mortality than the nondelirious group. Just over half of the delirious group died. Delirium developed within an average of 2 days of initial COVID-19 symptom onset, with symptom onset to ED within an average of 4 days, and symptom onset to death within an average of 11 days. Consistent with research on delirium due to COVID-19 and other etiologies, our research suggests that hypoactive delirium is the most common delirium subtype in the older ED patient (Evensen et al, 2018; Han et al, 2009; Kennedy et al, 2020).

Presentations of delirium without respiratory symptoms were seen in 18 individuals (26%), and delirium as the only presenting symptom in six (9%). All six individuals with delirium as the only presenting symptom of COVID-19 in the ED had a prior history of delirium. Three of these individuals died, comparable to the mortality rate of the entire delirium sample, although symptom onset to death occurred within an average of 4 days, implicating a high risk of rapid deterioration in these individuals.

Our results are largely consistent with those of prior studies and suggest that delirium is a common, early occurring, and lethal manifestation of COVID-19 in older adults who present to the ED, in most cases causing acute on chronic neurocognitive dysfunction strongly influenced by inflammatory and hypoxic-ischemic mechanisms. Given the significantly increased risk of mortality in these individuals, a simple risk tool could be used to predict delirium in older adults presenting to the ED with COVID-19, providing an avenue for prevention and treatment to lower mortality.

Although delirium due to COVID-19 has similar risk factors as delirium due to other etiologies, there are several unique characteristics. COVID-19 is a respiratory illness that can present with delirium in the absence of respiratory symptoms, effectively disguising itself as a delirium due to a different etiology. In a subset of older adults with COVID-19 in the ED, delirium was the only presenting symptom. Delirium due to COVID-19 most commonly presents as a hypoactive state in the ED, making it less likely to be detected than hyperactive or mixed delirious states. Thus, regardless of symptomatology, clinicians need to remain vigilant of possible COVID-19 in older adults who present to the ED with decreased responsiveness. Finally, there are environmental factors unique to COVID-19 that potentially contribute to increased delirium risk, such as increased anxiety and social isolation resulting from a deadly pandemic, particularly in individuals residing in assisted living and nursing homes where lockdown measures were widespread.

Study Limitations

It is important to consider the present study in context of its limitations. Retrospective chart reviews are associated with underassessment and underdocumentation of delirium symptoms, potentially resulting in an underestimation of true base rates of delirium in similar samples. Our sample size was modest compared to other studies in this area and consisted of medically compromised older adults with high rates of dementia, many of whom were residing in assisted living or nursing homes—the initial epicenters of infection in our area.

Further, our data were gathered from a single hospital in an ethnically homogenous (predominantly White) region of the Northwest United States and included the first reported individuals with COVID-19 in the United States. In this early stage of the pandemic, there was a paucity of information regarding early recognition of COVID-19 and its diverse manifestations in older adults, and no predictive risk tools or available protocols specific for the prevention and management of delirium due to COVID-19 and the unique challenges it presents. These factors limit the generalizability of our findings to younger and healthier individuals, community-dwelling older adults, ethnically diverse individuals and geographic locations, and later stages of the pandemic.

CONCLUSION

Research investigating the long-term sequelae of COVID-19 in hospitalized older adults is quickly accumulating. Given the strong interrelationship between delirium and dementia, both clinically and pathophysiologically, these studies will likely reveal the secondary impact of delirium due to COVID-19: escalating dementia rates. Thus, prevention continues to be the ultimate goal.

Currently, the most effective strategy for reducing delirium due to COVID-19 remains the prevention of infection through vaccination, physical distancing, and mask use. In individuals with COVID-19 not requiring hospitalization, prevention of delirium involves early recognition and medical guidance, as well as reducing modifiable risk factors at home, such as dehydration, malnutrition, alcohol use, polypharmacy, poor sleep, social isolation, sensory deprivation, and reduced activity level. In hospitalized individuals, the prevention of delirium includes empirically supported interventions such as the ABCDEF bundle (Marra et al, 2017) and the Hospital Elder Life Program (Inouye et al, 1999). Difficulties implementing these established protocols during the COVID-19 pandemic have been outlined elsewhere with excellent solutions provided (Kotfis et al, 2020; LaHue et al, 2020).

Delirium prevention plans specific to COVID-19 are increasingly being developed, such as those focused on key nursing interventions intended to promote sleep, support adequate nutrition, encourage mobility, maintain or improve cognition, and enhance social support by engaging individuals in meaningful conversations and activities and facilitating virtual visitation with loved ones at least once daily (Radhakrishnan et al, 2021). Continued investigations of the

clinical and pathophysiological characteristics involved in the genesis of delirium due to COVID-19 are also very important to reduce acute risk and severity, thereby mitigating negative long-term outcomes before they occur, and furthering our understanding of delirium more generally.

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