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Brief Report

Altered Mental Status: An Important but Overlooked Presenting Symptom of COVID-19 in Older Adults

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ABSTRACT

Objectives: To determine whether altered mental status (AMS) as a presenting symptom in older adults with COVID-19 is independently associated with adverse outcomes. **Methods:** A retrospective single center observational study of admitted patients ($n = 421$) age greater than 60 and a positive COVID-19 test. Outcomes included mortality, intubation, acute respiratory distress syndrome, acute kidney injury, and acute cardiac injury. Multivariate regression analysis was used to determine if presenting with AMS was associated with adverse outcomes. **Results:** There was an increased risk of mortality (RR 1.29, 95% CI 1.05–1.57), intubation (RR 1.52, 95% CI 1.09–2.12) and AKI (RR 1.42, 95% CI 1.13–1.78) in patients that presented with AMS. **Conclusions:** During a global pandemic, prognostic indicators are vital to help guide the clinical course of patients, reduce healthcare cost, and preserve life. Our study suggests that AMS can play a major role in diagnostic algorithms in older adults with COVID-19. (Am J Geriatr Psychiatry 2021; 29:1166–1170)

Highlights

- Is altered mental status as a presenting symptom prognostic of adverse outcomes in older adults infected with COVID-19?

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- Older adults that have been infected with COVID-19 and present with AMS are at greater risk for mortality, intubation, and development of acute kidney injury than their non-AMS counterparts.
- Awareness of this risk can motivate timely preventative or treatment interventions that may improve the patient's clinical course, reduce healthcare cost burden and ultimately preserve life.

OBJECTIVES

Since its discovery, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has led to nearly one million deaths globally.¹ Several studies have indicated that the older adult population makes up a large percentage of patients that are hospitalized, intubated, and ultimately die.²

In older adults, altered mental status (AMS) is a well-recognized presenting symptom in infections, particularly pneumonia. It is well known that AMS can serve as a gauge of disease severity in older adults.³ Despite this, there has been a lack of attention paid to AMS as a presenting symptom of COVID-19 in older adults. The purpose of this study is to elucidate the association of AMS as a presenting symptom of COVID-19 and adverse outcomes in older adult COVID-19 positive patients.

METHODS

Study Design

This is a retrospective observational study of patients tested for COVID-19 at SUNY Downstate Health Sciences University in New York. Testing was conducted via nasopharyngeal swab and subsequent reverse-transcription polymerase chain reaction. Patient data was collected from the Healthbridge Electronic Medical Record System and deidentified into a secure database. The Downstate Institutional Review Board approved this study for publication, informed consent was waived given the retrospective nature of this study.

Study Sample

This study cohort had 683 patients who were tested for COVID-19 and 421 patients were ultimately used for analysis. The population included patients

60 years of age or older who were admitted from March 10, 2020 to April 13, 2020. Patients were excluded from the study if their COVID-19 test was negative; if they were less than 60 years of age, or if they had major variables missing (Supplementary Fig. 1). Patients were classified as having AMS on presentation based patient admission notes that explicitly stated "altered mental status" or "AMS" or a Glasgow Coma Scale of less than 15. The primary outcome was 30 day in-hospital mortality. Secondary outcomes included intubation status, Acute Respiratory Distress Syndrome (ARDS), acute kidney injury (AKI) and acute cardiac injury (ACI). AKI and ARDS were defined using the KDIGO criteria and Berlin criteria respectively. ACI was defined as a troponin above the 99th percentile of the upper reference limit in less than 30 days of COVID-19 diagnosis.

Statistical Analysis

General participant demographics and characteristics were expressed as mean (SD) if normally distributed or median (IQR) if not. Differences in demographics, clinical characteristics, and outcomes were compared between the group that presented with AMS and the group that did not present with AMS using bivariate analysis (Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables). p-value of <0.05 was determined to be of significance. Log-binomial regression models were used to determine if presenting with AMS was associated with an increase in relative risk of outcomes upon adjustment for covariates. Covariates were selected a priori based on known or established risk factors for the outcome of interest in the setting of COVID-19. These included age, sex, and comorbidities (diabetes, hypertension, obesity) as they have been independently associated with mortality and intubation, in addition to renal disease for AKI. All statistical analysis was performed using SAS Studio 3.8 software.

RESULTS

Of the total sample (n = 421), 202 (48.0%) patients died and 219 (52%) were discharged. 161 (38.2%) patients had AMS on admission. 58.4% of patients that presented with AMS died during hospitalization compared to 41.5% of those that presented without AMS. Of the total patients, 29 (6.2%) of patients presented with AMS as their sole presenting symptom and 47 (11.2%) presented with AMS lacking typical symptoms including fever and shortness of breath. Patients that presented with AMS were older, had lower median admission temperature, and had significantly more history of CVA and CKD than the non-AMS presentation group (Supplemental Table 1).

Multivariate regression analysis revealed that AMS and age were independently associated with mortality, AMS and obesity were independently associated with intubation, and AMS and male sex were independently associated with AKI (Table 1). AMS did not demonstrate an association with the outcomes of ACI or ARDS.

CONCLUSIONS

To our knowledge, this is one of the first studies to report the increased risk for mortality, intubation, and AKI in an older adult subset presenting with AMS. The causes of AMS in the setting of COVID-19 are likely due to a multitude of factors, including dehydration, cytokine storm, hypoxia, fevers, metabolic imbalances, and possibly more directly through viral invasion of the central nervous system.⁴ Several studies have postulated that the disruption of brain stem neurons, either through direct infection or systemic complications of the virus may result in respiratory dysregulation.⁵ Although further investigation is needed, the association of AMS with mortality and intubation found in our study may be explained by the ensuing respiratory collapse and hypoxia caused by such a manifestation of the virus. Furthermore, several studies have reported the incidence of AKI in the setting of COVID-19. It is hypothesized that AKI occurs due to both direct viral infiltration of tubular epithelium and podocytes, as well as indirectly, through systemic complications caused by the virus.⁶

TABLE 1. Relative Risks for Association Between AMS and Mortality, Intubation and Acute Kidney Injury

Predictor	Relative Risk With 95% CI	Wald x ²	p-Value
AMS and Mortality (unadjusted)	1.41 (1.16-1.71)		0.0006
AMS and Mortality (adjusted)	1.29 (1.05 – 1.57)	6.07	0.014
Age ^a	1.02 (1.004 – 1.03)	7.08	0.008
Male versus Female	1.12 (0.92 – 1.37)	1.38	0.24
Hypertension	0.84 (0.66 – 1.06)	2.11	0.15
Diabetes mellitus	1.09 (0.89 – 1.33)	0.69	0.41
Obesity (BMI > 30)	1.04 (0.85 – 1.28)	0.16	0.69
AMS and Intubation (unadjusted)	1.40 (1.00 - 1.97)		0.05
AMS and Intubation (adjusted)	1.53 (1.11 – 2.10)	6.02	0.01
Age ^a	1.00 (0.99 – 1.01)	8.80	0.42
Male versus Female	1.34 (0.98 – 1.81)	1.58	0.06
Hypertension	0.96 (0.63 – 1.47)	2.67	0.85
Diabetes mellitus	1.24 (0.91 – 1.69)	0.36	0.18
Obesity (BMI > 30)	1.59 (1.17 – 2.16)	4.46	0.003
AMS and AKI (unadjusted)	1.45 (1.15-1.83)		0.001
AMS and AKI (adjusted)	1.42 (1.13 – 1.78)	9.03	0.003
Age ^a	1.01 (1.00 – 1.02)	2.81	0.09
Male versus Female	1.30 (1.03 – 1.64)	4.96	0.03
Hypertension	1.24 (0.83 – 1.86)	1.13	0.29
Diabetes mellitus	1.27 (0.99 – 1.64)	3.47	0.06
Obesity (BMI > 30)	1.22 (0.98 – 1.52)	3.09	0.08
Renal disease	1.10 (0.87 – 1.40)	0.61	0.43

^a Age is used here as a continuous variable so with every one unit increase in age there is a 1.02 times greater risk of death. Note: Log binomial regression analysis was used to compute relative risk for outcomes of interest. Degree of Freedom = 1. Note: Covariates included Age, Sex, Hypertension, Diabetes Mellitus and Obesity for the outcomes of mortality and intubation. The aforementioned covariates in addition to renal disease were used in the AKI model.

AKI is a known cause of delirium and coma in patients that are severely ill, and it is plausible that the association between AMS and AKI found in our study is due to AMS being an early finding of kidney injury in patients with COVID-19.⁷

While the cause of AMS in the setting of COVID-19 has yet to be determined, its impact on mortality, intubation, and AKI in our study was significant and should be interpreted as a prognostic indicator of adverse outcomes in older adults. A study by Chen et al. reported that patients with “disorder of consciousness” were more prevalent in patients that died from the infection (20%) than in those that did not (1%).⁸ In our study we noted higher numbers; 58.4% of patients that succumbed to illness presented with AMS. Additionally, the risk of dying in patients with COVID-19 presenting with AMS was 29% greater compared to those that did not present with AMS, even after adjusting for possible influencing factors such as comorbidities and age. We also found that the risk of intubation in older adults presenting with AMS in the setting of COVID-19 was 58% greater when compared to those that did not, a finding that is yet to be reported. Although the aforementioned risk values are not very large, given the gravity of the outcomes of interest (mortality and intubation), and the impact of such outcomes on public health in the setting of the COVID-19 pandemic, these findings should be considered clinically significant and addressed as such. Furthermore, we also found that the risk of developing AKI was 42% greater in patients that presented with AMS compared to those that did not, another novel finding. Finally, 6.2% of our older adult patients presented with AMS as their only symptom, while 11.1% presented with AMS while lacking typical symptoms of fever and SOB, giving some credence to the hypothesis of Ward et al that in some older adults, AMS may be the earliest sign of COVID-19 infection even before respiratory symptoms develop.⁹

There are several limitations to this study. First, probable delirium has been found to be associated with frailty in older adults with COVID-19, and it is possible that our patients that presented with AMS may have had higher frailty scores which resulted in adverse outcomes.¹⁰ We were unable to assess clinical frailty scale due to insufficient data recorded in charts during the peak of the pandemic. Second, the baseline mental status was unknown in our patient

population, which could contribute to a change in the rate of AMS documented. Lastly, our study sample is not generalizable to the U.S. population because our patients are from a single hospital system in a predominantly low-resourced community with poor access to social determinants of health. Yet, this allows it to be generalizable to similar communities.

Despite these limitations, our study also has notable strengths. We are among the first to report an association between AMS and mortality, intubation and AKI in an older adult patient population with COVID-19. Additionally, we supplement the growing literature on disorders of consciousness such as delirium as a predictor of adverse outcomes in older adults with COVID-19, but focus on the broader presenting symptom of AMS, thereby aiding clinicians that may be unable to screen using DSM-5 criteria in time constricted surge situations. Given these findings, it is imperative that AMS be recognized as an alarming presenting symptom of COVID-19 and prognostic indicator of adverse outcomes in older adults. National guidelines, such as the United States Centers for Disease Control and Prevention (CDC) make no mention of AMS in their screening criteria. This is especially concerning given that routine screening for COVID-19 such as temperature checks can have limited efficacy in older adults. Cardinal signs of infection such as fever can be absent or blunted in older adult patients with infection. Adding AMS as an important presenting symptom of COVID-19 will ensure early identification and treatment of disproportionately affected patient populations such as older adults.

AUTHOR CONTRIBUTIONS

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DISCLOSURE

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SUPPLEMENTARY MATERIALS

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