



# Neurological manifestations in 404 COVID-19 patients in Washington State

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Dear Sirs,

We report neurological manifestations in 404 consecutive patients with COVID-19 seen in outpatient clinics and hospitalized between February 20, 2020 and May 4, 2020 at Evergreen Hospital, Kirkland, Washington, USA. This hospital was among the first to report cases and deaths of COVID-19 patients in the United States. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most neurological manifestations of COVID-19 have been reported from non-USA health systems for hospitalized patients [1–3].

All patients had laboratory confirmed SARS-CoV-2 infection. Only new onset neurological manifestations were included. Study data were extracted from electronic medical records, and all neurological manifestations were confirmed via chart review by a neurologist and neuropsychologist. The study was approved by institutional review board and ethics committee. Core presenting symptoms were fever, cough, and shortness of breath.

Clinical characteristics and admission laboratory measures are summarized in Table 1. Shapiro's test revealed significant deviations from normal distribution. Therefore, non-parametric alternatives to the *t* test (Wilcoxon rank sum test and Hodges–Lehmann estimation) were used, at alpha level of 0.05, adjusted for multiple comparisons using the Benjamini–Hochberg method.

Female patients younger than 65 years old were more likely to have neurological symptoms; however, the findings were not statistically significant. Asian patients were 2.02 times more likely to have neurological symptoms than

Caucasian patients, but the findings did not meet statistical significance either.

Frequencies of neurological symptoms are summarized in Table 2. Neurological findings were reported in 295 of 404 (73.0%) patients, which is higher than reported by the previous studies from China and Spain [1, 3]. Mao et al. reported neurological manifestations in 36.4% of a sample of hospitalized patients from Wuhan, China [1] and Romero-Sánchez et al. reported neurological manifestations in 57.4% of a sample of hospitalized COVID-19 patients in Spain [3]. Helms et al. reported neurological signs in 84% of hospitalized patients in France; however, this was in a subset of patients with severe SARS-CoV-2 infection in intensive care, frequently under general anesthesia [2].

In our study, 208 of 404 (51.5%) patients presented with Central Nervous System (CNS) symptoms. The most prevalent CNS symptoms were altered mental status (86, 21.3%), headache (82, 20.3%), and dizziness (31, 7.7%). Of the 86 patients with altered mental status, 49 (57.0%) had pre-existing dementia. Out of 404 patients, 163 (40.3%) presented with Peripheral Nervous System (PNS) symptoms. The most prevalent PNS symptoms were myalgia (131, 32.4%) and impairment of taste (27, 6.7%) and smell (18, 4.5%).

Acute neurological manifestations were seen in 99 of 404 (24.5%) COVID-19 patients with altered mental status seen in 86 (21.3%), critical illness myopathy in 8 (2.0%), stroke including one hemorrhagic stroke in 3 (0.7%), and seizures in 2 (0.5%). Six patients had multiple acute neurological manifestations.

This study is useful to inform clinicians treating COVID-19 patients about neurological manifestations, which may be overlooked due to life-threatening acute respiratory complications. The common occurrence of neurological manifestations in outpatient clinics is important to recognize as being related to COVID-19 to initiate early intervention and prevent community spread. Altered mental status may be the presenting symptom of COVID-19, particularly in patients with pre-existing dementia.

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**Table 1** Clinical characteristics and admission lab measures of all COVID-19 patients

Characteristics	Without neurological symptoms (109 patients)	With neurological symptoms (295 patients)	<i>p</i> values	Odds ratio		
	No. (%) of patients	No. (%) of patients				
<b>Age, year<sup>a</sup></b>						
≥ 65	52 (12.9)	129 (31.9)	0.55	1.17 (0.75, 1.82)		
< 65	57 (14.1)	166 (41.1)				
<b>Gender</b>						
Male	48 (11.9)	149 (36.9)	0.30	0.77 (0.50, 1.20)		
Female	61 (15.1)	146 (36.1)				
<b>Race</b>						
Caucasian	93 (23.0)	237 (58.7)	0.18	NA		
African American	5 (1.2)	6 (1.5)		0.39 (0.14, 1.48)		
Asian	5 (1.2)	31 (7.7)		2.02 (0.88, 5.75)		
Native Hawaiian or Pacific Islander	0 (0.0)	4 (1.0)		1.56 (0.19, 66.5)		
American Indian or Alaska Native	0 (0.0)	3 (0.7)		1.17 (0.14, 53.87)		
Undetermined	6 (1.5)	14 (3.5)		0.78 (0.34, 2.28)		
<b>Core symptoms</b>						
Fever <sup>b</sup>	60 (14.9)	194 (48.0)	0.75	NA		
Cough	76 (18.8)	212 (52.5)		0.86 (0.58, 1.27)		
Shortness of breath	57 (14.1)	166 (41.1)		0.90 (0.59, 1.37)		
<b>Preadmission comorbidities</b>						
Cardiovascular disease <sup>c</sup>	31 (7.7)	63 (15.6)	0.02	NA		
Peripheral vascular disease	1 (0.2)	21 (5.2)		5.08 (1.29, 39.3)		
Dementia <sup>c</sup>	21 (5.2)	34 (8.4)		0.75 (0.40, 1.58)		
COPD <sup>c</sup>	17 (4.2)	41 (10.1)		1.10 (0.58, 2.38)		
Diabetes mellitus <sup>c</sup>	12 (3.0)	48 (11.9)		1.79 (0.91, 4.09)		
Chronic kidney disease	14 (3.5)	36 (8.9)		1.16 (0.59, 2.63)		
Asthma	8 (2.0)	17 (4.2)		0.91 (0.41, 2.57)		
Cancer	4 (1.0)	17 (4.2)		1.65 (0.63, 5.92)		
Hypertension <sup>c</sup>	16 (4.0)	52 (12.9)		1.48 (0.78, 3.17)		
Rheumatoid arthritis	6 (1.5)	4 (1.0)		0.28 (0.10, 1.23)		
Others	1 (0.2)	10 (2.5)		2.42 (0.60, 20.3)		
<b>Admission lab measures, median (range)</b>						
	Without neurological symptoms median (interquartile range)	With neurological symptoms median (interquartile range)		Confidence intervals	<i>p</i> value	Reference range
White blood cell count/ $\mu$ L	7630 (5815–11,710)	6470 (4935–9680)		– 2050.00 to 269.99	0.48	4000–9000
Absolute neutrophil count/ $\mu$ L	4910 (4090–7950)	4730 (3320–7895)	– 1500.00 to 389.99		1780–5380	
Absolute lymphocyte count/ $\mu$ L	960 (710–1260)	990 (747.5–1315)	– 129.99 to 190.00	0.92	1320–3570	
Absolute platelet $10^3/\mu$ L	223 (168–295.5)	204 (154–262)	– 46.99 to 12.99	0.53	163–337	
C-reactive protein, mg/dL	9.82 (3.21–15.02)	8.02 (4.82–13.04)	– 3.38 to 3.51	0.92	≤ 01.50	
Lactate dehydrogenase(U/L)	314 (281.25–414.75)	366.5 (343.75–457.25)	– 39.99 to 163.99	0.48	100–200	
Aspartate aminotransferase, U/L	36 (25.5, 56)	34 (25, 51)	– 7.99 to 5.00	0.92	5–40	
Alanine aminotransferase, U/L	24 (15.5, 47.5)	25 (17, 40.75)	– 6.00 to 5.00	0.92	5–50	
Blood urea nitrogen, mmol/L	15 (9.5, 27)	19 (13, 30)	0.00 to 6.99	0.48	7–23	
Creatinine, $\mu$ mol/L	0.9 (0.7–1.25)	1.0 (0.8, 1.3)	– 0.00 to 0.20	0.50	0.7–1.5	
Creatine kinase, U/L	108 (76–184)	111 (65, 224)	– 37.99 to 37.99	0.92	35–232	

<sup>a</sup>The median age of the patients was 61 years<sup>b</sup>Patient complaint of fever<sup>c</sup>The most common comorbid conditions

**Table 2** Frequency of the neurological symptoms in COVID-19 patients

Nervous system symptoms	
All	295 (73%)
CNS <sup>a</sup>	208 (51.5%)
Dizziness	31 (7.7%)
Headache	82 (20.3%)
Altered mental status	86 (21.3%)
Acute cerebrovascular disease (Stroke)	3 (0.7%)
Gait imbalance	20 (5.0%)
Seizure	2 (0.5%)
PNS <sup>a</sup>	163 (40.3%)
Taste impairment	27 (6.7%)
Smell impairment	18 (4.5%)
Vision impairment	5 (1.2%)
Nerve pain	1 (0.2%)
Myalgia	131 (32.4%)
Rhabdomyolysis	4 (1.0%)
Critical illness myopathy	8 (2.0%)

<sup>a</sup>More than one clinical symptom was present in 61 CNS and 21 PNS patients

## Compliance with ethical standards

**Conflicts of interest** The authors report no conflict of interest.

**Ethical standard statement** Study is in compliance with ethical standards.

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