Journal of Neurological Disorders

J Neurol Disord
Volume 11:2, 2023

Research Article

Open Access

Application of CURB-65 for Determining the Prognosis of Hospitalized Covid-19 Patients with Neurological Symptoms

Fahimeh Vahabizad[1,2], Zahra Ebadi[2], Mansoureh Togha[2,3*], Mohammad Reza Fattahi[2,4], Sima Naeini[1,2], Maryam Karaminia[1,2] and Seyedeh Melika Hashemi[2]

[1]*Department of Neurology, Tehran University of Medical Sciences, Iran*
[2]*Department of Headache, Tehran University of Medical Sciences, Iran*
[3]*Department of Headache, Iranian Center of Neurological Research, Iran*
[4]*Department of Surgery, Tehran University of Medical Sciences, Iran*

Abstract

Objective: Covid-19 patients can show various neurological symptoms. We aimed to assess the disease severity and prognosis in Covid-19 patients who experienced neurological symptoms.

Methods: In this retrospective, cross-sectional study, we evaluated 225 hospitalized Covid-19 patients with neurological symptoms. Their CURB-65 scores were measured to determine their pneumonia severity in relation to their neurological symptoms.

Results: The patients had different types of neurological symptoms, among which an altered level of consciousness was the most common (62.1%), followed by headache (50.7%). Patients with headaches had ultimately an 80% lower mortality rate ($p \leq 0.001$). Patients who were conscious at the time of admission were 62% less likely to die ($p=0.019$). Based on the CURB-65 severity score, most patients (40.4%) were in the mild group, 33.8% were in the moderate group and 25.8% in the severe group. The presence of headache at admission was inversely related to the CURB-65 score, meaning that a patient with early-onset headache recorded a lower CURB-65 score ($p \leq 0.001$; $r=-0.389$).

Conclusion: Neurological symptoms are a common part of the Covid-19 clinical spectrum. The severity of Covid-19 varied in patients exhibiting different neurological symptoms. A more severe disease course was observed with altered mental status and a milder course with headache at admission.

Keywords: Covid-19 • Neurological symptoms • Leukoaraiosis • Disease severity • Mortality • CURB-65

Introduction

The involvement of Covid-19 disease caused by SARS-CoV-2 is not restricted to the respiratory system; both the peripheral and central nervous systems can be affected. It has been shown that Covid-19 patients can demonstrate neurological manifestations such as altered consciousness, headache, dizziness and seizure [1]. Although some studies have shown that the clinical course of Covid-19 is more severe in patients who experience neurological symptoms, other studies have indicated that not all neurological symptoms worsen the prognosis [2]. It is imperative for both the patient and the physician to gain insight into the prognostic values of different neurological symptoms.

Thus far, several prognostic tools have been evaluated for determining Covid-19 clinical course and severity, such as CURB-65. CURB-65 has been found to be a valid and simple tool for the determination of the severity of Community-Acquired Pneumonia (CAP). A few studies have used CURB-65 for risk stratification of Covid-19 patients [3,4]. In the present study, we aimed to determine the severity of Covid-19 disease in patients who exhibited neurological symptoms and to use the measurement of CURB-65 as a prognostic marker in these patients.

***Address for Correspondence:** Mansoureh Togha, Department of Headache, Tehran University of Medical Sciences, Iran, Email: toghae@sina.tums.ac.ir*

Received: 27-March-2023, Manuscript No. jnd-23-94869; **Editor assigned:** 29-March-2023, PreQC No. P-94869 (PQ); **Reviewed:** 12-April-2023; QC No. Q-94869; **Revised:** 17-April-2023; Manuscript No. R-94869 (R); **Published:** 24-April-2023, **DOI:** 10.4172/2329-6895.11.2.545

Methods

In this retrospective, cross-sectional study, we evaluated 225 Covid-19 patients exhibiting neurological symptoms at Sina Hospital, which is affiliated with Tehran University of Medical Sciences. The study was approved by the ethics committee of Tehran University of Medical Sciences (IR.TUMS.NI.REC.1400.010). The Covid-19 diagnosis was confirmed by a positive result from a nasopharyngeal SARS-CoV-2 PCR or by having both typical respiratory symptoms and lung involvement in a chest CT.

The patient demographic features, clinical characteristics, prognosis, laboratory results and imaging findings were extracted from a pre-designed electronic database. The neurological symptoms were recorded as headache, decreased level of consciousness, vertigo, ataxia, dizziness, Focal Neurological Deficit (FND), seizure and delirium. A decreased level of consciousness was defined as any decrease in the Glasgow coma scale. The presence of aphasia, paresis, dysarthria, hemianopia, cranial nerve palsy or hemi-sensory impairment was regarded as a FND. A diagnosis of delirium was based on DSM-5 criteria as a fluctuating disturbance of attention and awareness along with additional cognitive impairment (e.g., perception, memory deficit, language, disorientation, visuospatial ability) that developed within a short period of time and could not be explained by a neurocognitive disorder or deep coma. The Covid-19 prognosis was assessed based on the presence of mortality, end-organ damage acute liver failure, acute renal failure, ARDS, acute cardiovascular damage, hematological abnormalities) and the need for mechanical ventilation.

Imaging tests included chest and brain CT scan and all biochemical assessments (complete blood cell count, blood chemical analysis,

coagulation testing, assessment of liver and renal function testing, C-reactive protein, creatine kinase and lactate dehydrogenase) were performed according to the clinical care needs of the patient. Chest CT involvement was categorized as mild, moderate, or severe using a semi-quantitative scoring system.

To calculate CURB-65 for each patient, one point was added for each of the following features that were present: confusion (mental test score ≤ 8 for new disorientation in person, place or time), BUN 20 mg/dL, respiratory rate ≥ 30 breath/min, blood pressure (systolic<90 mmHg or diastolic ≤ 60 mmHg), age ≥ 65 years. The CURB-65 was interpreted as follows: 0-1: probably suitable for home treatment; low risk of death; 2: consider hospital supervised treatment; ≥ 3: manage in hospital as severe pneumonia with a high risk of death.

The collected data were analyzed using SPSS software version 26. Because the distribution of objects was not normal in the statistical population, the nonparametric Mann-Whitney U and regression tests were used. A p-value of <0.05 was considered statistically significant.

Results

A total of 225 Covid-19 patients with neurological symptoms were evaluated, among which 58.2% were male and 41.8% were female. The mean age of the patients was 60.75 ± 16 years. The baseline characteristics of patients are recorded in Table 1.

Table 1. Patients baseline characteristics

		N (%) or Mean (SD)
Sex	Male	131(58.2)
	Female	94 (41.8)
Age (years old)	Female	62.2 (15.8)
	old)	59.7 (16.3)
Total		60.75 (16.0)
Vital Sign	Systolic Blood Pressure (M)	126.3 (25.7)
	Diastolic Blood Pressure (M)	77.3 (15.2)
	Oxygen Saturation (M)	90.4 (8.6)
	Respiratory Rate (N)<24	180 (89.6)
	Respiratory Rate (N)>24	21 (10.4)
	Pulse Rate(N)<125	217 (98.2)
	Pulse Rate(N)>125	4 (1.8)
	Fever(N)	121 (54)
Clinical Neurological manifestation	Altered Consciousness (GSC<15)	139 (62.1)
	Headache	114 (50.7)
	Vertigo	21 (9.3)
	Dizziness	19 (8.4)
	Seizure	14 (6.2)
	Delirium	8 (3.6)
	Focal Neurologic Deficit	7 (3.1)
	Ataxia	3 (1.3)
Past Medical History	Comorbidity	151 (67.1)
	Hypertension	90 (40.2)
	Gastrointestinal Disease	75 (33.3)
	Diabetes	67 (29.8)
	Cerebrovascular Disease	40 (17.9)
	Liver Disease	17 (7.6)
	Chronic Kidney Disease	13 (5.8)
	Asthma	7 (3.1)
	Malignancy	7 (3.1)
	Lung disease	5 (2.2)
	End-Stage Renal Disease	5 (2.2)
	Rheumatologic Disease	4 (1.8)

Upon admission, the average oxygen saturation in the patients was 90% and about 54% of patients had a fever. The most common comorbidity among patients was hypertension (40.2%).

The patients showed different neurological symptoms, the most common of which was a decreased level of consciousness (62.1%), followed by headache (50.7%). Other neurological findings were vertigo (9.3%), dizziness (8.4%), seizure (6.2%), delirium (3.6%), FND (3.1%) and ataxia (1.3%). The length of the hospital stays varied and averaged 6.3 days. Most patients did not require mechanical ventilation (78.7%). About 10% of patients developed end-organ damage and 15% of patients eventually died.

No significant relationship was observed between gender and mortality (p=0.46). End-organ damage and mortality were more prevalent in patients who received mechanical ventilatory support p (p ≤ 0.001, r=0.374 and p ≤ 0.001, r=0.718, respectively). The risk of death was higher in older patients (p=0.028). Most patients (40.4%) were in the mild group, followed by 33.8% and 25.8% in the moderate or severe groups, respectively. Regression analysis performed on patient vital signs at admission indicated that those with a respiratory rate of more than 24 per minute were 3.6 times more likely to die (p=0.011).

Individuals with higher oxygen saturation had significantly lower mortality rates (p=0.004). A pulse rate of more than 125 beats per minute and fever did not increase mortality (p=0.781 and p=0.962, respectively). Systolic and diastolic blood pressure were also significantly lower in patients who ultimately died (p=0.031 and p=0.051, respectively). However, according to regression analysis, these two factors could not predict death (p=0.843 and p=0.307, respectively).

The regression analysis on the non-neurological extra-pulmonary symptoms upon admission indicated that those with gastrointestinal (GI) symptoms, including nausea, vomiting, abdominal pain, diarrhea, and anorexia, were 4.1 times more likely to die (p ≤ 0.001). In the regression evaluation of neurological symptoms at the time of admission, the presence of headache was related to an 80% lower mortality rate (p ≤ 0.001). The presence of headache on arrival also reduced the risk of mechanical ventilation support by 69% (p=0.002). Patients who were conscious at the time of admission were 62% less likely to die (p=0.019). None of the neurological factors at the onset of admission predicted end-organ damage.

In patients who ultimately died, leukocytosis (WBC>11,000) was significantly higher (p ≤ 0.001) and serum lymph was substantially lower (p=0.004). Patients with leukocytosis demonstrated a 4.4-fold increase in the likelihood of death. Serum WBC (direct, p=0.003), serum lymph

(inverted, p=0.012), ALT (direct, p ≤ 0.001) and AST (direct, p=0.023) were significantly associated with end-organ damage. Blood sugar levels of more than 140 mg/dl upon admission were associated with a 4.9 times greater risk of end-organ damage.

Of the patients, 160 underwent a CT scan of the lungs before treatment, all of whom showed various degrees of pulmonary involvement. The details are reported in Table 2.

Table 2. Imaging findings and laboratory results

N (%)			Serum Findings	Mean ± SD (Mode)
Chest CT	Mild Involvement	34(21.3)	WBC (103/L)	8.4 ± 5.7
			Lymphocyte (%)	20.1% ± 11.2
	Moderate Involvement	61(38.1)	Hemoglobin (gr/dl)	13.4 ± 2.2
			Platelet (103/L)	222.7 ± 98.1
	Severe Involvement	65(40.6)	Glucose (mg/dl)	149.4 ± 89.9
			BUN (mg/dl)	40.1 ± 39.6
Brain CT	Valid CT scan	18 (100)	Creatinine (mg/dl)	1.3 ± 1.0
				135.2 ± 10.1
	Normal CT/ Nonspecific findings	4 (22.2)	Potassium (mEq/L)	4.3 ± 0.6
			Calcium (mg/dl)	8.7 ± 0.8
	New vascular event	14 (77.8)	PT (second)	15.2 ± 4.6
			PTT (second)	34.5 ± 15.2
Brain MRI	Valid MRI 19 (100)		INR	1.5 ± 0.3
			AST (U/L)	56 ± 30.7
			ALT (U/L)	42.7 ± 29.3
	Normal MRI/Nonspecific findings 12 (63.2)		LDH (U/L)	581.7 ± 243.5
			CPK (U/L)	295 ± 402.3
			D-dimer (ng/ml)	1914.13 ± 2277.9
	New vascular event	7 (36.8)	Ferritin (ng/ml)	535.8 ± 589.2
			Troponin (ng/l)	403.5 ± 2918.0
Nasoph aryngeal PCR	7 (36.8)	7 (36.8)	ESR (mm/h)	48.8 ± 32.8
	Positive	139 (66.5)	CRP	62.9 ± 54.3
	Negative	70 (33.5)		

Note: CT: Computed Tomography; SD: Standard Deviation; MRI: Magnetic Resonance Imaging; PCR: Polymerase Chain Reaction; BUN: Blood Urea Nitrogen; PT: Prothrombin Time; PTT: Partial Thromboplastin Time; INR: International Normalized Ratio; AST: Aspartate Transaminase; ALT: Alanine Transaminase; LDH: Lactate Dehydrogenase; CPK: Creatine Phosphokinase; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein

Subgroup analysis indicated that patients with severe lung involvement were 5.4, 2.7, and 3.8 times more likely to exhibit end-organ damage, requirement of ventilation, and mortality, respectively (p=0.002; p=0.011; p=0.001, respectively).

The CURB-65 score was used to evaluate the severity of pneumonia among the 225 cases in this study. Most patients (40.4%) were in the mild group, followed by 33.8% in the moderate and 25.8% in the severe group. Figure 1 shows the distribution of patients in the different CURB-65 classifications for surviving and non-surviving groups. The lowest score was 0 and the highest was 4, with the average score being 1.74 ± 1.12. Those who achieved a score of 4 were about 4.7 times more likely to require mechanical ventilation and 4.7 times more likely to die than patients with a score of 0 (p=0.041). In these patients, there was no significant relationship between this score and the length of hospital stay (p=0.64). Fever (body temperature ≥ 38) and decreased blood oxygen saturation at arrival significantly increased the severity score in these patients (p=0.027, and p=0.002, respectively) (Figure 1).

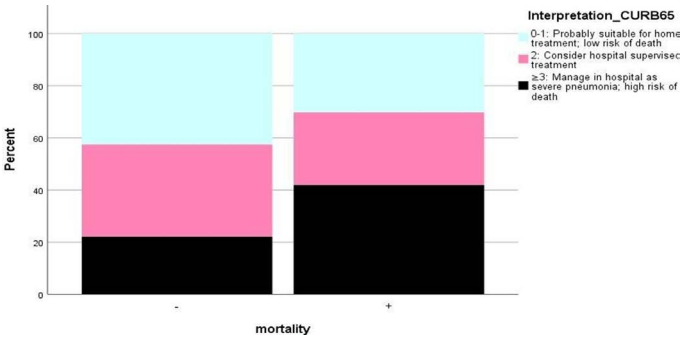

Figure 1. Stacked bar percent of mortality by interpretation of CURB-65

Discussion

In the present study, the relationship between Covid-19-related neurological symptoms and the severity of Covid-19 was examined using the CURB-65 scores to discover the role of the selected neurological symptom for predicting the Covid-19 severity. A recent study evaluated the performance of CURB-65 for predicting the mortality of Covid-19 patients within one month. In their study, 80.8% of patients had a CURB-65 score of 0-1 and 19.2% had a CURB-65 score of ≥ 2 [5]. In another study, CURB-65 was measured in 271 hospitalized Covid-19 patients and 61.3% had scores of 0-1, 23.7% of 2 and 15.1% of ≥ 3 [6].

In the present study, most patients (40.4%) were considered to be low risk (CURB-65=0-1), 33.8% to be intermediate risk (CURB-65=2), and 25.8% to be high risk of 30-day mortality (CURB-65 ≥ 3). Compared to previous studies, it appears that the percentage of patients who were considered to be low-risk (CURB-65) was lower in the present study. Considering that the subjects in this study were Covid-19 patients with neurological symptoms, it appears that COVID-19 related neurological symptoms intensified the Covid-19 severity.

In terms of the non-neurological extra-pulmonary symptoms of our patients, gastrointestinal symptoms showed a direct relationship with mortality. Studies have shown a conflicting association between GI symptoms and Covid-19 severity and mortality. Pooled analysis from a recent meta-

analysis showed a higher prevalence of GI symptoms in severe Covid-19 patients. This meta-analysis indicated an attenuated risk of mortality in Covid-19 patients presenting with GI symptoms compared to non-GI symptoms; however, their results were not significant [7].

It appears that, in some Covid-19 patients, there could be a temporal correlation between neurological and GI symptoms. This synchronicity between CNS and GI symptoms can be explained by several mechanisms, including shared angiotensin-converting enzyme 2 (ACE2) receptors in the GI and Central Nervous System (CNS), gut-brain axis involvement induced by inflammatory responses and the involvement of lateral nuclei of the hypothalamus linking to the GI tract by neural and hormonal mechanisms [8].

Overall, 62.1% of patients in the current study had some degree of disturbance in their level of consciousness, from mild drowsiness to deep coma. Generally, the mechanisms contributing to Covid-19 related altered levels of consciousness are multifactorial and include systemic metabolic and inflammatory changes, coagulopathy and direct invasion of the virus into the CNS [9]. In our study, mortality was lower in fully conscious patients. As expected, an altered level of consciousness showed a direct association with CURB-65 scores. Furthermore, the mortality rate was clearly higher in patients having a higher CURB-65 score. One study has reported that a decreased level of consciousness is an independent predictor of Covid-19 severity [10,11]. It can be concluded that an altered level of consciousness can be a valuable clinical predictor for Covid-19 prognosis.

Headache was the second most common symptom in our study (50.7%). One hypothesis for developing headache in the Covid-19 course is that the virus can directly affect the CNS through cranial nerves, particularly the trigeminal nerve [12]. However, it seems that direct invasion of SARS-CoV-2 into the CNS is rare. Headache attributed to systemic viral infections in the absence of meningitis or encephalitis is another possible explanation for Covid-19 related headache [12]. In the current study, those who reported headache at admission had a better prognosis (80% lower mortality rate) and Covid-19 patients with admission headache had lower CURB-65 scores.

In a recent case-control study, patients with headaches were more likely to have mild ARDS than those without headaches. Their study also showed that headache was associated with mild inflammation, mild pulmonary involvement and a better prognosis [13]. Previous studies have shown that Covid-19 patients presenting with myalgia and fever were more likely to report headache. All of these symptoms can be the result of activated lymphocytes and macrophages as well as the secretion of interleukins and interferons [14].

Except for headache and altered levels of consciousness, which were clearly associated with the CURB-65 score, we found no association between other neurological symptoms and CURB-65 scores. Furthermore, we assumed that the CURB-65 classification would not be a useful tool for predicting the prognosis of Covid-19, particularly in the first two stages in which there was no clear difference between the prognostic parameters. A recent study showed that CURB-65 classification was not useful in triaging Covid-19 for managing inpatients versus outpatients and this result is in agreement with the findings of our study [6]. However, it appears that relying on higher CURB-65 scores (4) compared to a zero score can be reasonable for predicting the risk of mortality.

There were some limitations to our study. Firstly, symptoms like headache and dizziness are subjective and their presence depend on the patient's ability to report them; therefore, these symptoms cannot be assessed in cases with mental status changes or in patients with respiratory devices that tend to impair communication. Secondly, our patients were sampled from hospitals rather than communities, which can lead to selection bias. The lack of a control group and a longer period of follow-up were other limitations.

Conclusion

Neurological symptoms are a common part of the Covid-19 clinical spectrum. The severity of Covid-19 in relation to different neurological symptoms varied. A more severe disease course could be seen for patients with mental status changes and a milder course for those reporting headache.

Funding

The authors received no specific funding for this article

Acknowledgement

None.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

All data not published within this article will be made available by request from any qualified investigator.

References

1. Whittaker, A, Anson M and Harky A. "Neurological Manifestations of COVID-19: A Systematic Review and Current Update." *Acta Neurologica Scandinavica* 142(2020): 14-22.
2. Orsucci, D, Ienco EC, Nocita G and Napolitano A, et al. "Neurological Features of COVID-19 and Their Treatment: A Review." *Drugs Context* 9(2020): 1-5.
3. Guo, J, Zhou B, Zhu M and Yuan Y, et al. "CURB-65 May Serve as a Useful Prognostic Marker in Covid-19 Patients within Wuhan, China: A Retrospective Cohort Study." *Epidemiol Infect* 148(2020): e241.
4. Carriel, J, Jaramillo MR, Ladinez BO and Villacreses HF, et al. "CURB-65 as a Predictor of 30-day Mortality in Patients Hospitalized with Covid-19 in Ecuador: COVID-EC Study." *Rev Clin Esp* 222(2021): 37–41.
5. Satici, C, Demirkol MA, Altunok ES and Gursoy B, et al. "Performance of Pneumonia Severity Index and CURB-65 in Predicting 30-day Mortality in Patients with Covid-19." *Int J Infect Dis* 98(2020): 84-89.
6. Nguyen, Y, Corre F, Honsel V and Curac S, et al. "Applicability of the CURB-65 Pneumonia Severity Score for Outpatient Treatment of COVID-19." *J Infect* 81(2020): e96-e98.
7. Menon, T, Sharma R, Earthineni G and Iftikhar H, et al. "Association of Gastrointestinal System with Severity and Mortality of Covid-19: A Systematic Review and Meta-Analysis." *Cureus* 13(2021): e13317.
8. Bostancıklıoglu M. "Temporal Correlation between Neurological and Gastrointestinal Symptoms of SARS-CoV-2." *Inflamm Bowel Dis* 26(2020): e89-e91.
9. Liotta, EM, Batra A, Clark JR and Shlobin NA, et al. "Frequent Neurologic Manifestations and Encephalopathy-associated Morbidity in Covid-19 Patients." *Ann Clinic Translat Neurol* 7(2020): 2221-2230.
10. Liang, W, Liang H, Ou L and Chen B, et al. "Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients with Covid-19." *JAMA Intern Med* 180(2020): 1081-1089.
11. Garcez, FB, Aliberti MJ, Poco PC and Hiratsuka M, et al. "Delirium and Adverse Outcomes in Hospitalized Patients with Covid-19." *J Am*

Geriatr Soc 68(2020): 2440-2446.

12. Bolay, H, Gul A and Baykan B. "Covid-19 is a Real Headache!" *Headache* 60(2020): 1415-1421.
13. Martinez, GA, Fanjul V, Ramos C and Ballesteros SJ, et al. "Headache during SARS-CoV-2 Infection as an Early Symptom Associated with a More Benign Course of Disease: A Case–Control Study." *Eur J Neurol* 28(2021): 3426-3436.
14. Trigo, J, Azorín GD, Gomez PA and Pías ME, et al. "Factors Associated with the Presence of Headache in Hospitalized Covid-19 Patients and Impact on Prognosis: A Retrospective Cohort Study." *J Headache Pain* 21(2020): 1-10.

How to cite this article: Vahabizad, Fahimeh, Ebadi Z, Togha M and Fattahi MR, et al. "Application of CURB-65 for Determining the Prognosis of Hospitalized Covid-19 Patients with Neurological Symptoms." *J Neurol Disord*. 11 (2023):545.