Clinical Characteristics and Functional Outcomes of COVID-19 Patients with Acute Ischemic Stroke

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Introduction

- Neurological complications frequently occur in patients with COVID-19 infection, affecting up to 57% of patients[1].
- SARS-CoV-2 has been shown to induce a state of hypercoagulability that predisposes to both arterial and venous thrombotic events[2].
- Stroke appears to complicate 0.2 to 5% of COVID-19 infections [1,3,4].
- Patients with vascular risk factors associated with stroke, such as hypertension, diabetes mellitus, and previous cardiac or cerebrovascular disease are at an increased risk of mortality and morbidity[5-8].

Background and purpose

- In this study, we describe the clinical characteristics and functional outcomes of stroke in patients with COVID-19 infection and evaluate the hypothesis that COVID-19 infection worsens the prognosis of patients with a stroke, possibly due to harmful effects of the virus.

Methods

- We conducted a prospective, observational, single-center cohort study at King Abdullah University Hospital (KAUH), the main tertiary hospital in North of Jordan.
- The recruitment of patients began on October 16th, 2020, and ended on October 15th, 2021.
- All patients diagnosed with acute ischemic stroke and COVID-19 infection were included. Patients were identified by neuroimaging studies and included in the study if the imaging showed acute ischemic stroke and classified according to the nucleic acid amplification tests as COVID-19 positive or COVID-19 negative.
- Patients underwent a standard diagnostic evaluation, including brain imaging, intracranial and extracranial vascular imaging, and cardiac evaluation.
- All patients presenting with hemorrhagic stroke or transient ischemic attack were excluded. The ischemic stroke subtype was classified according to the Trial of ORG 10172 in Acute Stroke Treatment Criteria (TOAST).



Results

- A total of 178 patients with radiologically proven ischemic stroke were included with a mean (SD) age of 67.3 (12), and more than half of the cases were males (96/178; 53.9%). Thirty-six cases were COVID-19 positive related and had a mean (SD) age of 70 (11.5). Out of 19 cases of mortality, 15 (79%) occurred in the COVID-19 positive group.
- Laboratory results at admission showed that COVID-19 positive patients had a significantly higher median C-reactive protein levels (P < .001) and Erythrocyte sedimentation rate (P < .001), also, coagulation profiles showed that COVID-19 positive patients had a significantly higher median prothrombin time (P < .001) and D-dimer levels (P < .001) as well.
- When compared to COVID-19 negative patients, COVID-19 positive patients were more likely to be admitted to the ICU (41.7% vs. 4.9%; p <.001) and were more likely to have a higher median NIHSS score at baseline (11 vs. 6; p = .043), after 72 hours (12 vs. 6; p = .006), and at discharge (16 vs. 4; p <.001).
- They were also more likely to have a higher median mRS score after three months follow-up (p <.001).
- COVID-19 positive patients also had a higher rate of hemorrhagic transformation (16.7% vs 1.4%; P <.001), a higher median hospital stays (P < .001), and a higher mortality rate (41.7% vs 2.8%; P < .001). The detailed univariate analysis between the COVID-19 positive and COVID-19 negative stroke patients is represented in **Table 1**.
- As for the etiology of the strokes, COVID-19 positive patients had more strokes attributed to cryptogenic (50% vs. 10.6%) and cardioembolic (27.8% vs. 7%) causes, and less attributed to lacunar (8.3% vs. 54.2%), atherothrombotic (8.3% vs. 23.9%), and other determining causes (5.6% vs. 6.3%; P < .001 for the overall comparison), **Figure 1**.
- The multivariate analysis showed that an increase in the NIHSS score at admission was associated with an increase in the likelihood of having unfavorable outcome after three months. (OR=1.387, 95% CI [1.238 – 1.553]; P < .001). While having COVID-19 infection didn't impact the likelihood of having an unfavorable outcome significantly (OR=1.098, 95%CI [0.270 – 4.473]; P = .896).

Variables	Total patients, n = 178	Non-COVID-19, n = 142	COVID-19, n = 36	p-value
Demographics				
Age, mean ± SD	67.3 ± 12	66.6 ± 12.1	70 ± 11.5	.121
Gender (male), n (%)	96 (54)	76 (54)	20 (56)	.674
NIHSS score				
Baseline NIHSS, median (IQR)	7 (4-12)	6 (4-11)	11 (5-13.5)	.043
At 72 h, median (IQR)	7 (5-11)	6 (5-10)	12 (4.5-16)	.006
At discharge, median (IQR)	4 (2-11)	4 (2-8)	16 (3.5-22)	<.001
mRS score				
mRS at discharge, median (IQR)	2 (1-3)	2 (1-2)	2 (1-3)	.092
mRS after 3m follow-up, median (IQR)	3 (1-4)	2.5 (1-4)	4 (2-6)	<.001
Unfavorable functional outcome, n (%)	95 (53)	71 (50)	24 (67)	.073
Metrics				
Stroke Unit admission, n (%)	155 (87)	135 (95)	20 (56)	<.001
ICU admission, n (%)	22 (12)	7 (5)	15 (42)	<.001
Hemorrhagic transformation, n (%)	8 (5)	2 (1)	6 (17)	.001
Hospital stay (days), median (IQR)	4 (3-8)	4 (3-6)	10 (4-16)	<.001
Deaths, n (%)	19 (11)	4 (3)	15 (42)	<.001

Table 1: General demographics and clinical data of the whole cohort, and it's stratification based on the COVID-19 infection status..

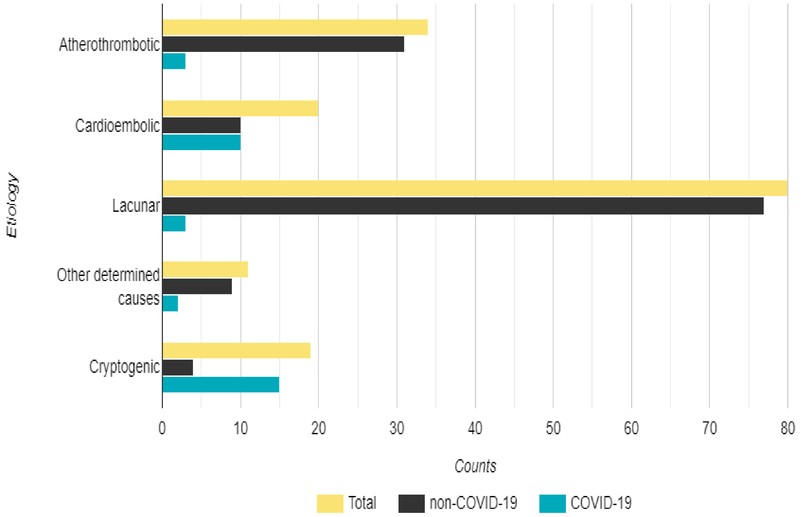


Figure 1: Distribution of the strokes based on etiology.

Conclusions

- Patients with ischemic strokes occurring with concomitant COVID-19 infection have more severe strokes and unfavorable functional outcomes after three months of follow-up, when compared with COVID-19 negative.
- The pathophysiology behind strokes occurring in COVID-19 patients remains not fully understood. Therefore, future controlled, prospective international studies with a higher sample size are needed to establish an evidence-based approach to stroke occurring in COVID-19 patients and elaborate more on their outcomes.

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